

**ANNIVERSARY REVIEW**

Hans-Georg Rammensee · Thomas Friede
Stefan Stevanović

MHC ligands and peptide motifs: first listing

Received: 13 December 1994

Introduction

The purpose of this article is to provide a compendium of major histocompatibility complex (MHC) peptide motifs and MHC ligands known to date, together with a discussion of the methods used to gain this information. A problem here is the exponential growth of information in this field over the recent years. The number of known MHC ligands was zero in 1989 and three in 1990. This article, written in 1994, lists a couple of hundred such ligands, plus a large number of likely ligands. By the time this work is published, we expect a lot more ligands to be known. On the other hand, the peptide motifs of many of the more important MHC class I molecules are known already, so that this article will still be useful as a source of information. For class II, the situation is a bit different. Only a few allele-specific motifs have been reported, and the data from different authors are partially conflicting. The principles of allele-specific ligand motifs, however, have emerged recently by the combination of information on MHC class II structure, ligand sequencing, and peptide binding assays. Thus, these principles can be applied to further ligands to be identified.

Overview of MHC function

MHC molecules are peptide receptors. Their function is to collect peptides inside the cell and to transport them to the cell surface, where the complex of peptide and MHC molecule may be recognized by the T-cell receptor (TCR) for antigen of T lymphocytes (Rammensee et al. 1993). In normal cells, MHC-associated peptides are derived from normal, that is, self proteins. During their differentiation,

T cells become tolerant to complexes of self peptides and self MHC molecules (Von Boehmer 1992). Thus, if any new peptides, e.g., derived from an infectious agent, occur later, they can be recognized by T cells. Since the specific immune system is regulated by T cells, the trimolecular complex of TCR, MHC molecule, and peptide can be considered a control switch for the immune system. Thus, a study of the molecular interactions between the three parts is essential for our understanding of the immune system.

Two classes of MHC molecules are distinguished, class I and class II. Class I molecules consist of a membrane-inserted heavy chain of about 45000 M_r , and a non-covalently attached light chain of 12000 M_r (Klein 1986). The latter is also known as β_2 -microglobulin (β_2m). The structure of class I molecules has been resolved by X-ray crystallography (Stern and Wiley 1994). It has some resemblance to a moose's head, whereby the antlers would form a groove that is recognized as a peptide-binding device. HLA-A, B, and C are the "classical" class I molecules of humans, and H-2K, H-2D, and H-2L those of the mouse. Class II molecules are heterodimers consisting of two chains α and β , of similar size (about 30000 M_r), both of which are membrane inserted. HLA-DR, DQ, and DP are the human class II molecules, H-2A and E those of the mouse. Their structure is surprisingly similar to that of class I molecules (Stern and Wiley 1994; Stern et al. 1994; Brown et al. 1993).

All HLA molecules, including the numerous "non-classical", are encoded on chromosome 6, with the exception of β_2m which is on chromosome 15. H_2 genes are on chromosome 17 of the mouse, and the mouse β_2m gene is on chromosome 2.

A peculiarity of MHC genes is their extensive polymorphism, characterized by the presence of dozens or hundreds of alleles in a species. H_2 alleles are designated H_2K^b , H_2K^d , H_2K^k and so on for class I, and H_2A^b , H_2A^k , H_2Ab^k , H_2Eb^d and so on for class II, whereby different alleles may differ in as many as 40 amino acids (Klein 1986). The present nomenclature (Bodmer et al. 1994) of HLA genes and products (which has been changed several times) is outlined as follows: class I heavy chain

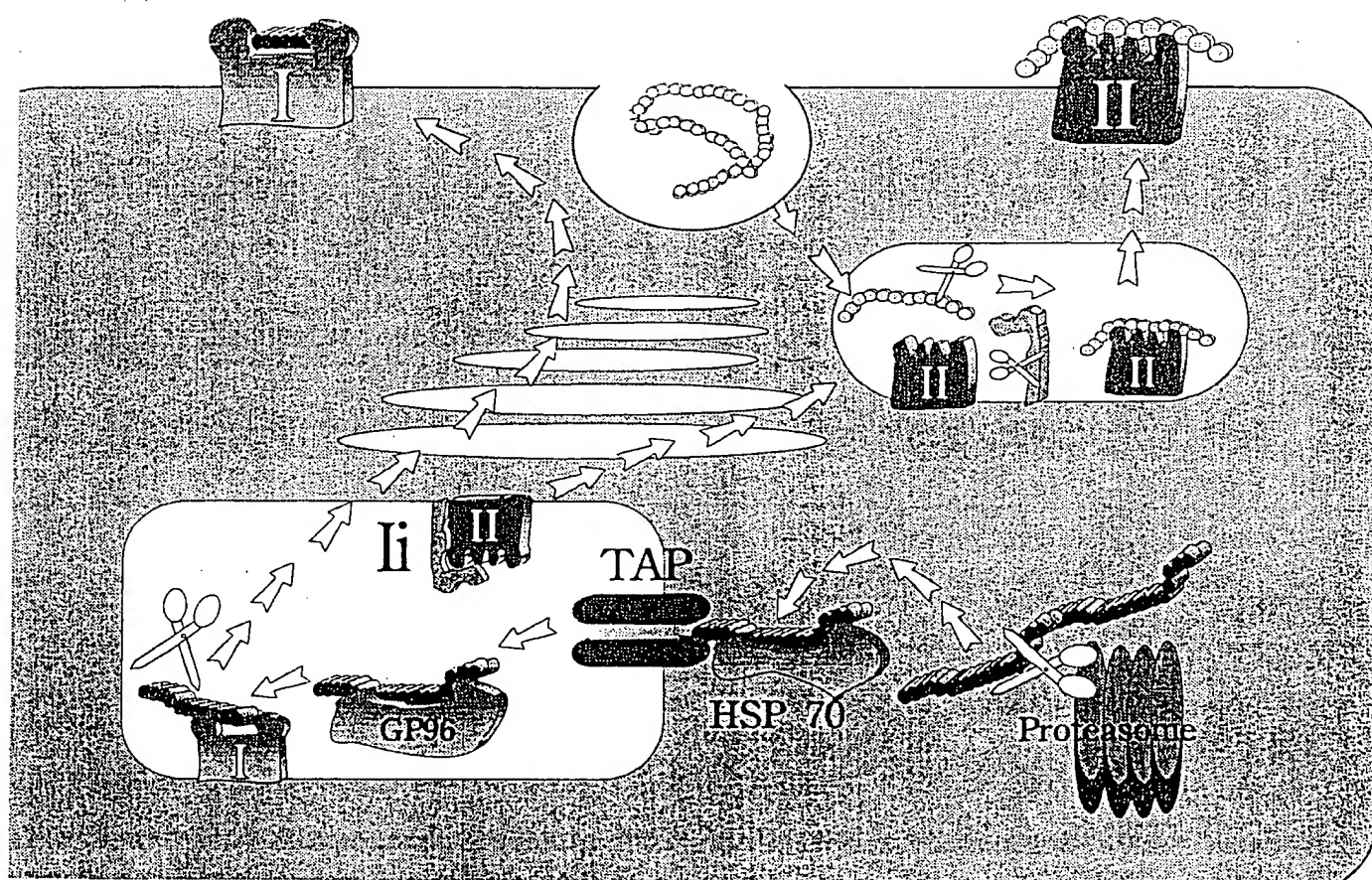


Fig. 1 A simplified and partially hypothetical overview of antigen processing. For explanation see text

loci: *HLA-A*, *B*, and *C*; class II α chain loci: e.g., *HLA-DRA*, *DQA1*, *DPA1*, class II β chain loci: e.g., *HLA-DRB1*, *DRB3*, *DQB1*, *DPB1*. Alleles are designated, for example, *HLA-A*0201*, or *HLA-DRB1*0101*. This nomenclature can only be applied if the respective sequences are known. Since this is not the case in many situations, the old designations, e.g., *HLA-A2* or *HLA-DR3*, based on serology, are still being used, and describe collections of alleles with shared serologic determinants (e.g., *HLA-A2* for *A*0201* through *A*02012*). Both class I light chains and *HLA-DR α* chains are not very polymorphic (Klein 1986). The high (*HLA-B*) or at least moderate polymorphism of the other genes results in the expression of a large number of combinations of alleles at the different loci per chromosome (haplotype), and in a high degree of heterozygosity. Thus each individual has his or her particular combination of HLA molecules, namely up to six different class I and about six different class II molecules (if the non-classical HLA molecules, whose function is not known, are not considered), making it unlikely to find two unrelated individuals with exactly the same combination of *HLA* genes.

A simplified outline of MHC function is given in the diagram in Figure 1. Class I molecules, both heavy and light chains, are synthesized into the ER (reviewed in Jackson and Peterson 1993). The peptides to be loaded on class I molecules are, in many cases, derived from cytosolic

proteins. The details of peptide generation are not known definitely. A widely held view, however, is that cytosolic proteins are partially degraded by an endopeptidase activity of the proteasome, a multiunit structure with several activities located in the cytosol (Rock et al. 1994). It is not clear, however, how the products of such endopeptidase activity are related to the final class I ligands (Dick et al. 1994). One possibility is that the proteasomes directly produce the correct ligands. Alternatively, proteasomes could cut out larger peptides requiring further processing. The endopeptidase specificity of the proteasome is such that a protein is cut after hydrophobic or charged residues, in principle. The fine specificity of endopeptidase activity is influenced by two proteasome subunits, LMP2 and LMP7, which are encoded in the MHC region and regulated by IFN. However, the exact kind of LMP influence on specificity is controversial (Howard and Seelig 1993). In any case, such peptides must be transported into the ER lumen by the TAP molecule [(transporter associated with processing) (Neefjes and Momburg 1993)]. According to one hypothesis, these peptides are bound and protected from complete degradation by a chaperone, HSP70, before reaching TAP (Srivastava et al. 1994). Peptide transport by TAP molecules has

been directly demonstrated recently (reviewed in Momburg et al. 1994). Transport has specificity especially regarding the C-termini of peptides, and selectivity for peptide lengths. Peptides of 7 to 23 amino acids have been shown to be transported, whereby optima of 10 to 15 amino acids are seen. Human TAPs do not discriminate much between the C-termini of peptides. In contrast, the mouse TAP has a preference for peptides with hydrophobic C-termini and dislikes peptides with charged termini. This pattern of specificities fits well with the peptide specificities of human and mouse MHC class I molecules, since all mouse class I molecules require peptides with hydrophobic C-termini, whereas some human class I molecules require peptides with basic C-termini. On the other hand, mouse cells transfected with the *HLA-A3* gene, requiring peptide ligands with basic C-termini, can be loaded with the fitting peptides (Maier et al. 1994). This indicates that MHC peptide specificity need not be strictly dependent on TAP specificity. That TAP specificity indeed can influence MHC peptide loading is evident from two different TAP forms in the rat, TAP^a and TAP^b. Dependent on co-expressions of the respective TAP, the peptide spectrum of rat MHC class I molecules, RT1^u, is different, as indicated by different HPLC behavior of RT1^u-associated peptides. When measured in a peptide transporter assay, TAP^a has the same specificity as human TAP, that is, it does not discriminate between hydrophobic and basic C-termini, whereas TAP^b is more like the mouse transporter, with a preference for peptides with hydrophobic C-termini.

Once they are inside the ER lumen, the further fate of transported peptides is not exactly known. The recently reported physical association of TAP molecules and class I molecules suggested that peptides are directly loaded onto class I molecules immediately after discharge from the transporter (Ortmann et al. 1994; Suh et al. 1994). However, this would require that either the incoming peptides are already of the right size for loading to class I molecules, or that they bind as longer peptides (Falk et al. 1990) and are trimmed while somehow bound to MHC. An alternative hypothesis is that peptides are first bound by a chaperone, gp96, which shuttles the peptides to class I molecules, perhaps with some trimming of peptides underway. The main reason for assuming that gp96 plays a role in antigen processing stems from an impressive series of experiments by Srivastava and co-workers (1994), showing that gp96 molecules are associated with a large array of peptides and are able to immunize mice against antigens presented by MHC class I molecules.

In any event, the peptide somehow reaches the class I molecule and binds into the groove, perhaps after a final trimming step while already in touch with MHC. Unusually long peptides found associated with MHC class I molecules might have escaped such a final trimming (Urban et al. 1994). The assembly sequence of class I heavy chain, β_2m and peptide is not quite clear. A recent report indicates that another chaperone, calnexin, is bound to assembled complexes of heavy chain and β_2m , and thus retains empty class I molecules in the ER (Jackson et al. 1994). It is only upon peptide loading that the fully assembled heavy chain/

β_2m /peptide complex is released by calnexin for transportation to the cell surface.

Class II molecules also start their existence in the ER. The two chains, α and β , assemble and are bound by a chaperone-like molecule, the invariant chain [(Ii) (Cresswell 1994)]. This molecule has two functions; one is to direct the $\alpha\beta$ -heterodimer to the class II loading compartment, which appears to be a specialized vesicle characterized by the presence of class II molecules. The second function of Ii is the prevention of premature peptide loading to class II molecules. The molecular interactions between Ii and the $\alpha\beta$ -heterodimer preventing peptide binding are not completely sorted out; one possibility is an allosteric effect of Ii on the dimer such that the peptide binding groove is closed due to conformational change. The other possibility is that a particular stretch of the invariant chain binds into the groove and thereby competitively prevents the binding of peptides. This latter view is derived from the observation that Ii peptides, called CLIPs (class II-associated invariant chain peptides) are frequently found associated with immunoprecipitated class II molecules, and that CLIPs are especially abundant in cells with a defect in antigen processing. In any case, Ii is removed from the $\alpha\beta$ -heterodimer in the class II loading compartment, or shortly before. The peptides loaded onto class II molecules can be derived not only from endocytosed protein but also from protein endogenous to the cells, especially membrane-bound proteins which have a chance to co-localize in the class II loading compartment. Finally, the peptide-loaded $\alpha\beta$ -heterodimers are translocated to the cell surface.

The simplified view shown in Figure 1 suggests a strict separation of the processing pathways for class I and class II, respectively. There is strong evidence, however, for considerable cross-talk between the two pathways. Peptides derived from cytosolic proteins, for example, can be loaded onto class II molecules (Pinet et al. 1994). On the other hand, peptides derived from phagocytosed proteins can be loaded onto class I molecules, especially if the phagocytosed protein is aggregated (Pfeifer et al. 1993; Rock et al. 1993). Such side-lines of processing pathways deserve interest because they could be exploited for new strategies of immune intervention.

Methods of characterizing MHC/peptide interactions

The most seminal approach to gain information on the function of MHC molecules as peptide receptors is the X-ray analysis of MHC crystals (Stern and Wiley 1994). The two other principle methods are: 1) Biochemical isolation and study of naturally MHC-associated peptides, and 2) Binding studies with synthetic peptides. The latter two approaches are discussed below:

1) Analysis of natural MHC ligands

The diagram in Figure 2 gives an overview on the approaches used for isolation and analysis of MHC-associated peptides.

The major technical challenge is the small copy number of individual peptides. It is estimated that a cell presents well over 1000 different peptides on its 100 000 or so copies of a given MHC allelic product. A few of these peptides are present in high copy number, that is, up to 10 000 or more. By far the most ligands, however, occur in a much lower copy number, maybe even down to as low as one copy per cell.

The most sensitive means of detecting isolated peptides is the T-cell assay, which is able to detect peptides in the sub-picomolar range, at least as far as cytotoxic T cells are concerned (Rötzschke et al. 1990). Typically, a peptide-containing sample (e.g., a few μ l of an HPLC fraction) is incubated in a total volume of 100 μ l together with MHC-expressing, ^{51}Cr -labeled target cells. After some incubation time, e.g., 90 min, CTL are added, the supernatant is harvested 4 to 6 h later, and the relative radioactivity measured indicates the degree of target cell lysis. If the 100 μ l volume used for target cell incubation has a concentration of 1 pM, the absolute amount of peptide is 100 attomol, a sensitivity not reached by any other method. The use of the CTL assay, of course, is limited to the detection of T-cell epitopes for which T cells are on hand: Viral antigens, minor H antigens, tumor-associated antigens, transfected model antigens, or antigens recognized by alloreactive T cells. On the other hand, peptide detection assays for class-II-restricted T cells appear to be less sensitive than for class I-restricted T cells.

The major shortcoming of the T-cell assay for peptide detection is that it does not give sequence information. However, the location of a T-cell epitope among HPLC-separated MHC ligands of an infected cell can allow identification of the peptide in combination with biochemical analysis such as Edman degradation or mass spectrometry. The first naturally processed viral T-cell epitopes indeed were identified by the combination of T-cell assay with mass spectrometry, comparison of the HPLC behavior of synthetic and natural peptides, or partially direct sequencing, using radiolabeled amino acids incorporated by virus-infected cells (Rötzschke et al. 1990; van Bleek and Nathenson 1990). A combination of these methods for identification of T-cell epitopes is only possible if the proteins of origin are known. Direct sequencing of HPLC fractions containing a T-cell epitope is rarely successful, namely, only in cases where the T-cell epitope happens to be a peptide highly abundant in that fraction. A marked improvement of sensitivity was brought about by an ingenious combination of HPLC, CTL assay, and mass spectrometry by Cox and co-workers (1994).

By far the most ligands known to date are not T-cell epitopes and these ligands were determined by direct sequencing, either by Edman degradation, or by mass spectrometry, or by a combination of the two methods. Detection limit of Edman degradation is about 1 pmol, that

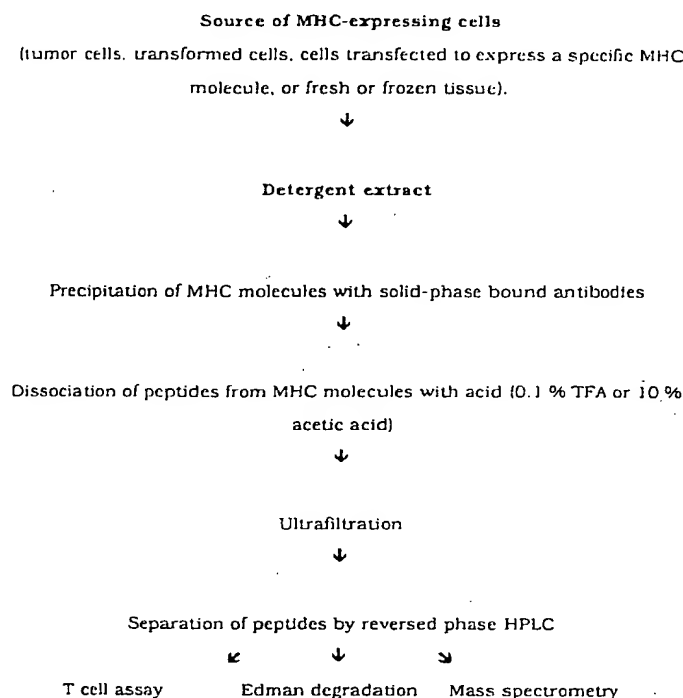


Fig. 2 Methods for analysis of MHC ligands

is, the equivalent of 6×10^9 cells for a peptide occurring in 100 copies per cell. Sequencing by tandem mass spectrometry has been reported to be more sensitive – down to 30 fmol or less. It is, however, challenging to achieve this degree of sensitivity, so that, apart from the pioneering group of Hunt and co-workers (1992), not many other laboratories have come up with similar results.

A special application of Edman degradation is pool sequencing, that is, altogether-sequencing of the complex mixture of peptides eluted from a given MHC species (Falk et al. 1991b). Although disliked by purists, this approach allows one to determine the common characteristics of all peptides associated with a given MHC molecule, with relatively little effort. Pool sequencing of MHC class I ligands led to the discovery of the principle of allele-specific motifs, and allowed a large number of such motifs to be determined. The clear information that can be obtained from pool sequencing of class I ligands is made possible by their uniform length, e.g., 9 amino acids. But even for class II ligands, which can range in length from about 12 to 25 amino acids, pool sequencing is a valuable tool for gaining detailed information on motifs (Falk et al. 1994b).

It appears that the number of amino acids between the N-terminus of class II ligands and the first anchor varies by about three amino acids for the majority of ligands. For DR1, for example, the distance from the N-terminus to the first anchor of the majority of ligands is 5 ± 1 (Falk et al. 1994b). Thus, pool sequencing indicates a cluster at position 4, 5, and 6 for the anchor residues used, aromatic and aliphatic. Again for DR1, the next cluster stretches over

positions 7, 8, and 9, indicating the next anchor for aliphatic residues. The rough motif obtained by such interpretations – absolute position 5 set as relative position 1 to mark the first anchor – can then be complemented and worked out in depth by applying 1) alignment of natural ligands, 2) consideration of the pockets, as revealed recently by crystallography of a monopeptidic DR1 molecule (Stern et al. 1994), and 3) considerations of peptide binding assays. If all four sources of information are considered, a detailed picture of the degenerate (as compared with class I) peptide specificities of class II molecules can be obtained that should be useful for epitope predictions (Friede and co-workers, submitted).

2) Peptide binding assays

MHC/peptide binding assays have a history of leading to obsolete results. On the other hand, with our increasing knowledge of MHC structure and MHC/peptide interaction and specificity, it is possible to design straightforward peptide binding experiments to answer specific questions. A number of approaches can be used to measure peptide binding to MHC. The oldest method is as follows (Buus et al. 1987): MHC molecules are purified and incubated with radioactively labeled peptides. Then the mixture is subjected to a gel filtration column. MHC molecules with the radioactive peptide bound will elute in the exclusion volume, whereas free peptides will elute later. Thus, the amount of radioactivity in the exclusion volume is a measure for peptides bound to MHC. The binding behavior of other, unlabeled peptides can be tested via their capacity to inhibit binding of the radioactive peptide. A number of variations of this method have been used. For example, the radioactive label can be replaced by a fluorescent marker. Furthermore, MHC/peptide complexes can be separated from free peptides by gel electrophoresis, or upon binding of the MHC/peptide complex to solid phase with the help of antibodies. In the latter case, however, two different antibodies reactive with different sites of the MHC molecule are required, one for purification of the MHC molecule, the other for capturing the MHC/peptide complex from the reaction mixture.

Depending on the conditions, these kinds of peptide binding assays can be made very sensitive to detect even low-affinity peptide binding. This may result in problems of interpretations, since low-affinity binding might not be relevant for physiological MHC/peptide interactions.

A second type of binding assay depends on the stabilization of MHC class I molecules by bound peptides. Cells with a defect in antigen processing, for example, TAP-defective RMA-S cells, express only a low density of antibody-detectable MHC class I molecules on their surface, if cultured under normal conditions (37 °C). If such cells are incubated with peptides binding to the expressed class I molecules with high affinity, the latter are stabilized, and their surface density increases (Townsend et al. 1989). Since determination of class I surface density can be easily done by FACS analysis, this approach has been widely

used. Since only few cell lines with transporter defects are known, the assay can only be used for MHC molecules expressed by such cells, e.g., H-2K^b or D^b for RMA-S cells. To study peptide binding for additional MHC-molecules, the desired MHC molecule can be expressed in RMA-S or other TAP-defective cells upon gene transfection. The advantage of this MHC-stabilization assay is that it is rather insensitive and thus detects only peptides binding with high affinity that are likely to be physiologically relevant. Stabilization of MHC molecules by peptides can also be measured with purified MHC molecules.

For class II molecules, the binding of high-affinity peptides leads to a compact form of the MHC/peptide complex, as seen by SDS gel electrophoresis, whereas a peptide of lower affinity leads to a "floppy" form of class II molecules.

A very elegant approach for studying the peptide specificity of class II molecules has been developed by Hammer and co-workers (Sinigaglia and Hammer 1994). A peptide library is expressed by bacteriophages. From the peptide-expressing phages only those are selected which are able to bind to a given class II molecule. The peptide sequences expressed by the selected phages are then determined. With this approach, a peptide binding motif of HLA-DR1 has been established that is well reflected among the natural ligands, and can be well explained by the crystal structure of HLA-DR1.

MHC class I ligands and motifs

The main purposes for which this information will be useful are the prediction of T-cell epitopes within proteins of known sequences and the detailed analysis of peptide/MHC interaction. For epitope prediction it is important not to consider just the basic motif of a given MHC molecule, since the non-anchor positions of peptides could also contribute considerably to the interaction with MHC. This is evident from the preferences seen for certain residues at non-anchor-positions in pool sequencing data, from the interaction of such residues with MHC sites as seen in crystals (Madden et al. 1993; Zhang et al. 1992; Fremont et al. 1992), and from detailed binding studies showing that certain residues at a given peptide position can be detrimental for binding (Ruppert et al. 1993; Kast et al. 1994; Parker et al. 1994).

The basic approach to search a protein sequence for an epitope fitting to a given class I molecule is as follows. First, the sequence is screened for stretches fitting to the basic anchor motif (2 anchors in most cases), whereby allowance should be made for some variation in peptide length as well as in anchor occupancy. If a motif, for example, calls for 9mers with I or L at the end, 10mers with a fitting C-terminus should be considered as well, and other aliphatic residues at the C-terminus, like Val or Met, should also be considered. In this way, a list of candidates will be obtained. These are now inspected for having as many non-anchor residues as possible in common with

ligands already known, or with the residues listed among the "preferred residues" or "others" on top of each motif Table. If possible, a binding assay can be performed at this stage to exclude weak binders which occur frequently among peptides conforming to a basic motif. If a detailed study on peptide binding requirements is available, the candidates can also be screened for non-anchor residues detrimental or optimal for binding (Ruppert et al. 1993; Kast et al. 1994; Romero et al. 1991; Ebert et al. 1993). One should keep in mind, however, that pure peptide binding motifs can be misleading in the search for natural ligands, since other constraints, such as enzyme specificity during antigen processing and specificity of transporters or chaperones, are likely to contribute to ligand identity in addition to the MHC binding specificity.

A careful consideration of the pocket structure of the MHC molecule of interest can also be useful for epitope prediction (Falk and Rötzschke 1993). For the P1 residue, for example, preferences can be explained by the residues contributing to the P1 contact site (Falk et al. 1995a,c). Since the MHC residues contributing to the different contact sites can differ among MHC molecules, such considerations should be held with caution, however (Guo et al. 1993). Computer modeling of the MHC molecule in question can be of help here.

The use of allele-specific peptide motifs is limited to a certain extent by exceptional ligands not fitting to a motif, e.g., Frumento and co-workers (1993) and Mandelboim and co-workers (1994). Such ligands will be missed by epitope predictions based on allele-specific motifs. It is not clear as yet how frequently this happens. In most cases, natural ligands will fit to the motifs, whereby substitutions of anchor residues with residues of similar chemistry (e.g., one aliphatic residue for another) and length variations are not infrequent and should be considered. A special case is the mouse H-2M3 molecule. A complete motif is not known, except that this molecule is specialized to present N-formylated peptides of bacterial or mitochondrial origin (Fischer-Lindahl 1991; Shawar et al. 1991).

MHC class II ligands and motifs

The long-awaited X-ray analysis of class II molecules has given us invaluable insight into peptide/class II interactions (Brown et al. 1993; Stern et al. 1994). Especially the detailed information on the 5 DR1-pockets accommodating anchoring side chains of one particular ligand, influenza haemagglutinin 306-318, provided a structural basis for the previously worked out peptide ligand motif of DR1 molecules (Rötzschke and Falk 1994; Sinigaglia and Hammer 1994). Moreover, pocket spacing and structure, as found for this one particular DR1/peptide complex, can be used to deduce the putative interaction for other DR1-peptide complexes and even for some other class II molecules. We found it particularly useful to evaluate pool sequencing data under the aspect of the expected pocket structure (Friede and co-workers, submitted; Schild and co-workers,

submitted). Combined with the alignment of individual class II ligands, this approach is a powerful tool to determine allele-specific class II peptide motifs, as we have exercised recently for several closely related DR4 subtypes (Friede and co-workers, submitted).

The general picture for allele-specific class II motifs emerging is as follows. A stretch of nine amino acids, on average starting at absolute positions 3 to 5 of natural ligands, is determined by the respective allele-specific motif, corresponding to the peptide portion embedded in the MHC groove. The first position of this nonamer stretch, P1, represents a hydrophobic anchor for all class II ligand motifs known so far. Anchoring of the hydrophobic P1 side chain in the respective class II pocket appears to be particularly intensive, as impressively illustrated by the deep pocket seen in the monopeptidic DR1 crystal. The importance of P1 side chains is also indicated by the striking influence of P1 on peptide binding, and by the significant clustering of hydrophobic residues at cycles 3 to 5 of self-peptide pools. In addition to P1, several other anchors follow up to P9. For DR1, these are at P4, P6, P7, and P9, as indicated by structural data, whereby the specificity of P7 is somewhat degenerate and escapes detection in binding assays or natural ligand analysis. For several other class II molecules, the same anchor spacing – P1, P4, P6, P7, P9 – is compatible with ligand motif data. DR2, DR3, and DR4 motifs as well as H-2E motifs fall into this category. Other molecules, like DR5, DPw4, and DQ7 appear to have slightly different anchor spacing, e.g., the second anchor at P3, or an anchor at P5. Allele-specific differences can occur at each of the anchor positions, although differences of P1 specificity in HLA-DR molecules are limited by the β 86Gly/Val polymorphism. More pronounced allele-specific differences are found for P4, P6, and P9, respectively. Charge differences are particularly evident; P4 of DR17, for example, requires Asp, whereas P4 of DR4Dw10 does not tolerate Asp or Glu but prefers basic or hydrophobic residues. P9, on the other hand, prefers hydrophobic residues for DR1 but negative charges for DR4Dw15 and positive charges for H-2E^k. Interestingly, charge differences in polymorphic stretches of class II molecules (probably reflecting counter charges for charged anchors) have been found to be associated with autoimmune diseases (Gregersen et al. 1987; Khalil et al. 1990; Todd et al. 1987).

Epitope prediction of class II ligands within a protein is not as easy as with class I, because the anchors, or interaction sites, are more degenerate in their specificity. The first step should be to pick out the most allele-specific anchor beyond P1, for example, P4 of DR17, P6 of DR1, or P9 of H-2E^k or DR4Dw15. The selection of nonamer sequences fitting to P1 and the other anchor of the respective motif is then further examined for adherence to the additional anchors. The resulting collection of nonamer stretches might then be inspected for adherence to the putative processing motif XPXX in the flanking regions (Rötzschke and Falk 1994). A quantitative ranking of the contribution of each amino acid residue at almost every position has been determined in an elegant approach by

Hammer and co-workers (1994) for DR4, which led to highly accurate predictions of good DR4 binders.

Technical notes

We have tried to put together all the motifs and natural ligands we were aware of. Due to the flood of data emerging in the past years, however, we anticipate that some information has been overlooked. We apologize in advance to those authors whose work was inadvertently not adequately covered.

In case of those class II ligands occurring as nested sets, we included only one or a few members of the set in many cases.

An X in peptide sequences stands for an undetermined amino acid. However, if the peptide sequence has been determined by mass spectrometry, as is the case for the peptides reported by Hunt and co-workers (1992a, b), X stands for either Leu or Ile (which have the same mass). Lowercase letters in peptide sequences indicate residue determination of lower confidence.

As far as T-cell epitopes are concerned, only those have been selected which are likely to be naturally processed;

criteria for judgement are to be found in Stevanović and Rammensee (1995). From the numerous class II motifs that have been published, we selected the more convincing ones, that is, those compatible with the class II structure. Due to the variable number of amino acids between the N-terminus and the first anchor of peptides, alignment of ligands or T-cell epitopes to class II motifs is always arbitrary, unless a structural analysis has been performed. For the class II molecules without reasonable motifs, a list of the published ligands is provided, without any attempt at alignment.

If you wish to have your motifs or ligands included in forthcoming listings, please send us reprints (no preprints) of the work describing them. We would also appreciate any comments on errors and omissions, as well as suggestions for improvements.

Acknowledgments The authors gratefully acknowledge the tremendous contributions of Kirsten Falk and Olaf Rötzschke to the original work covered. The original work from our laboratory was supported by grants from the Bundesminister für Forschung und Technologie, the Deutsche Forschungsgemeinschaft (Sonderforschungsbereich 120) and the Leibnizprogramm, and by Hoffman-La Roche Inc., Nutley, N.J. We thank Birgit Stiller and Anne Jordan for preparing the manuscript. The authors wish to thank all those who contributed unpublished and published information.

[illegible]

a: Falk et al. 1991 b; b: Röttschke et al. 1990; c: Falk et al. 1991 a; d: Harpur et al. 1993; e: Sibille et al. 1990; f: Wallny et al. 1992; g: Pamer et al. 1991; h: Pamer 1994; i: Braciale et al. 1987; k: Kuwano et al. 1988; l: Cao et al. 1994; m: Maryanski et al. 1986; n: Romero et al. 1989; o: Weiss et al. 1990; p: Kulkarni et al. 1993; q: Banks et al. 1993; r: Kutubuddin et al. 1992; s: Blum-Tirouvanziam et al. 1994; t: Townsend et al. 1994; u: Reich et al. 1994

Table 1 (Continued)
B H-2D^d

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		G	P		R K				I L F		a, b
Other preferred residues				D E Q		N I L	D E				
Examples for ligands	K	G	P	I	T	V	Q	I		Unknown	b
	V	G	P	Q	K	N	E	N	L	Unknown	b
	S	G	P	R	K	X	I	X	L	Homol. mRNA CD40 mouse	b
	A	G	P	D	R	T	E	K	X L	Unknown	b
	K	G	P	D	K	G	N	E	F	Homol. metalloproteinase 2 inhibitor	b
	I	G	P	E	R	G	H	N	L	Homol. hypoxanthine phosphoribosyl-transferase	b
	D	G	P	V	R	E	H	N	L	Homol. urease canavalia ensiformis	b
	K	G	P	E	R	X	N	G	L	Unknown	b
	S	G	P	E	R	G	E	K	L	Homol. proliferating cell nucleolar antigen P40	b
	D	G	P	V	R	G	I	S	I	Homol. ribosomal protein S17 rat	b
	N	G	P	Q	R	I	Y	N	L	Unknown	b
	S	G	P	V	A	L	V	N	F I	Unknown	b
	I	G	P	N	R	A	F	N	F	Unknown	b
	S	G	P	E	R	L	L	S	X Y	Homol. heterog. nucl. RNP complex K	b
	V	G	P	S	G	K	Y	F	I L	Unknown	b
	F	G	P	Y	K	L	N	R	L	Homol. feline leukemia virus envelope polyprotein	b
	F	G	P	L	K	F	N	V	L T	Unknown	b
	A	G	P	D	R	F	I	X	X M	Unknown	b
	F	G	P	Y	R	F	Y	V	L T	Unknown	b
	S	E	Q	D	L	N	F			Unknown	b
	S	X	H	K	E	Q	P	A	T	Homol. transforming protein spi-1 human	b
	S	X	P	K	T	D	X	Q	T L	Homol. insulin receptor precursor	b
T-cell epitopes		G	P	P	H	S	N	N	F G Y	Tum-P35B 4-13	c
	R	G	P	G	R	A	F	V	T I	HIV gp160 318-327	d, f
	L	M	G	Y	I	P	L	V	G A	HCV core 133-142	e

References:

a: Falk and co-workers, unpublished; b: Corr et al. 1993; c: Szikora et al. 1993; d: Takahashi et al. 1988; e: Shirai et al. 1994; f: Bergmann et al. 1993b

Table 1 (Continued)
C H-2L^d

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor residues		P S							F L M		a, b, c
Other preferred residues			G Q M L	T	T	I K F	F	Q N			
Examples for ligands		Y L L X A Q X X X Y X	P S S P P Q P P Q P N Q P	H P P L P Q P Q A N V K	F F F E A G R A S	M P P A M G R N L I A G	T D D N E R E Y P H G	N L* L* Q N N Q Y Y N F L	L* F F F L M	MCMV pp 89 168-176 OGDH 105-112 OGDH 97-112 Unknown Unknown Unknown Unknown Unknown Unknown Unknown Phosphoglycerate kinase 180-189	d e e c c c c c c c c
T-cell epitopes	V A I T R I E Q	R I L A Y T D S	P S P P P H P P	Q T Y T A L P V G	A Q N G A G P D R	S H N W A L R D S	G R L L H I L S	V A V E F G Y	M L F F F L L F	LCMV NP 118-126 Tumor antigen P91A 12-20 Tumor antigen P815 35-43 JHMV Nucleocapsid 318-326 Measles NP 281-289 E. coli β -gal. 876-884 Measles HA 343-351 Measles HA 544-552	f, g h i k l m n n

* Also a T-cell epitope

References:

a: Falk et al. 1991 b; b: Falk and co-workers, unpublished; c: Corr et al. 1992; d: Reddehase et al. 1989; e: Udaka et al. 1992; Udaka et al. 1993; f: Whitton et al. 1989; g: Schulz et al. 1991; h: Lurquin et al. 1989; i: Lethé et al. 1992; k: Bergmann et al. 1993 a; l: Beauverger et al. 1993; m: Gavin et al. 1994; n: Beauverger et al. 1994

Table 1 (Continued)
D H-2K^b

	Position								Source	Ref.
	1	2	3	4	5	6	7	8		
Anchor or auxiliary anchor residues			Y		F Y			L M I V		a
Other preferred residues	R I L S A	N	P	R D E K T		T I E S	N Q K			
Examples for ligands	R S H	G I I	Y I Y	V N E	Y F F	Q E P	G K Q	L* L* L	VSV NP 52-59 Ovalbumin 258-276 Unknown	b a, c, d n
T-cell epitopes	I S F K V Y F F	I S A G S G E E	Y I P P Y Q Q	R E N W J N T	F F Y F F R T	L A P P P A A	L R A T P D Q P*	I L L L G L A* P*	Rotavirus VP7 33-40 HSV glycoprotein B 498-505 Sendai virus NP 324-332 MuLV p15E 574-581 Rotavirus VP6 376-384 Rotavirus VP3 585-593 MUT 2 tumor antigen MUT 1 tumor antigen	e f g, h i, k l m m

* Also a T-cell epitope

+ One of these peptides was found in a total cell extract of K^b-expressing tumor cells

References:

a: Falk et al. 1991 b: van Bleek and Nathenson 1990; c: Rötzschke et al. 1991; d: Carbone et al. 1988; e: Franco et al. 1993; f: Bonneau et al. 1993; g: Kast et al. 1991; h: Schumacher et al. 1991; i: Sijts et al. 1994; k: White et al. 1994; l: Franco et al. 1994; m: Mandelboim et al. 1994; n: Wallny 1992

Table 1 (Continued)
E H-2D^b

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor residues					N				M I		a
Preferred residues		M	I L P V	K E Q V		L F					
Others	A N I F P S T V	A Q D	G	D T		A Y T V M E Q H I K P S	D E Q V T Y	F H K S Y			
Examples for ligands	A I	S Q	N V	E G	N N	M T	E R	T T	M* I*	Influenza A34 NP 366-374 Yersinia YOP 51 249-257	a, b, c n
T-cell epitopes	A S C Q S F S K R N	S A K G G Q G A A N	N I G I P V V H L	E N V N S E Y N D N	N N N N T N L N	M Y K L P G F I V R	D A E D A T V R	A Q Y N P G A T T D	M K L E I C G F (L)	Influenza A68 NP 366-374 SV 40 T 206-215 SV 40 T 223-231 SV 40 T 489-497 Adenovirus 5 E1A 234-243 LCMV NP 396-404 LCMV GP 276-286 LCMV GP 33-42 HPV16 E7 49-57 SV 40 T 492-500 (501)	d e, o e, o e, o f g h i, k l m

* Also a T-cell epitope

References:

a: Falk et al. 1991 b; b: Rötzschke et al. 1990; c: Townsend et al. 1986; d: Cerundolo et al. 1991; e: Deckhut et al. 1992; f: Kast et al. 1989; g: Yanagi et al. 1992; h: Oldstone et al. 1988; i: Oldstone et al. 1993; k: Klavinskis et al. 1990; l: Feltkamp et al. 1993; m: Alsheikly 1994; n: Starnbach and Bevan 1994; o: Tevethia et al. 1990

Table 1 (Continued)
F H-2K^b

	Position									Comments	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor residues	E									C-terminus at P8 or P9	a, b, c
Preferred residues	V F	D	K N Y M Q I L F P H T	L	A G P T V F S	N K H	T	I	I		
Examples for natural ligands	H D Y K E S S D E E	E D E E E E E E A	T H D M I V G G R T D P Y	T R T V V L G	F A G A K V G S H V K K	N G K K K R T K K	S I T I I I I I I	I I I I I I I I I		β Actin 275–282 S24 ribosomal protein 53–60 Unknown Homol. T cell transcript. factor 1 Hn RNP C protein 84–91 S7/S8 ribos. protein 137–144 H-2D ^b 112–119 Unknown CArG bind. factor A 209–216 BiP 158–165	k k k k k k k k k k
T-cell epitopes	F I S F S Y D T V E	E E D Y F N L E A E G	A G G S T L L D M E A G	N G G G T L L I Y E I A I	G W G R N L E Y K I V	N T L I K N H V	L G I K D G A V	I M I I K I I Q I		Influenza A HA 259–266 Influenza A HA 10–18 Influenza A NP 50–57 Influenza JAP HA 255–262 SV 40 T 560–568 P. falciparum CSP 375–383 P. falciparum CSP 371–379 HIV-1 RT 206–214 Rabies NS 197–205 Influenza A NSI 152–160	c, i c, i d, l e f g g h i a

References:

a: Cossins et al. 1993; b: Norda et al. 1993; c: Gould et al. 1991; d: Bastin et al. 1987; e: Sweetser et al. 1989; f: Rawie et al. 1988; g: Kumar et al. 1988; h: Hosmalin et al. 1990; i: Larson et al. 1991; Gould et al. 1987; k: Brown et al. 1994; l: Gould et al. 1989

G H-2K^{bm1}

	Position								Source	Ref.
	1	2	3	4	5	6	7	8		
Anchor or auxiliary anchor residues	E									a
Other preferred residues	Q G P	K N Q G M P Y	P	A R K			R Y			

References:

a: Norda et al. 1993

Table 1 (Continued)
H Qa-2

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		M L Q	N I L		V I I	K M I	H		L I F		a, b
Other preferred residues	K A E Q		T	P E A G K S D	L T E H M F Y	L F N Y	R	E Q N D K S T R			
Examples for ligands	K A K A K V R K A G I A S K K S Y D	Q L Q G L Q S L M Q L L Q V L	N A N L I N N L M N I L S L	P E P L K X G I A X E P I D P G	I L T G V T Q T K Y V D L M T	A P V M H Y H X H L V E T D M X H	H H R S H H H H Y R E H A X F N	Q E L S S P M L L Q I M L L L L	L <		

References:

a: Rötzschke et al. 1993; b: Joyce et al. 1994

I Selected other T-cell epitopes

MHC	Sequence												Comments	Ref.
H-2D ^k	R	R	K	G	K	Y	T	G	L				T cell epitope of LEC-A	a
H-2M3	fM	F	F	I	N	I	L	T	L	L	V	P	ND1α 1-17	b
	fM	F	F	I	N	A	L	T	L	L	V	P	ND1β 1-17	b

References:

a: de Bergeyck et al. 1994; b: Fischer Lindahl 1991

Table 2 HLA-A motifs
A HLA-A1

	Position									Source	Ref
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		T S	D E	P				L	Y		a, b, c, f, i
Other preferred residues		L		G I	G N Y	G V I					
Examples for ligands	A	T	D	F	K	F	A	M	Y	Cyclin-like protein 135-143	a, i
	I	A	D	M	G	H	L	K	Y	Proliferation cell nuclear antigen 241-249	a, b, i
	M	I	E	P	R	T	L	Q	Y	Ribosomal protein S16 40-48	a, b
	Y	T	S	D	Y	F	I	S	Y	Ets-1 154-162	a, i
	L	T	D	P	G	V	L	D	Y	Unknown	a
	V	S	D	I	V	G	P	D	G	Fibrillarlin 177-188	a, b
	Y	T	D	Y	G	G	L	I	F	Cytochrome C oxidase II	a, i
	Q	S	E	D	G	S	H	T	I	HLA class I α chain 111-123	a
	Y	L	D	D	P	D	L	K	Y	Cytosine methyl transferase 238-246	i
	S	T	D	H	I	P	I	L	Y	Fructose-6-amino transferase 217-225	i
	D	S	D	G	S	F	F	L	Y	IgG4 279-287	i
	G	T	D	E	X	R	N	X	Y	Unknown	i
	V	S	D	P	Y	N	X	K	Y	Unknown	d, i
	V	A	D	K	V	H	X	M	Y	Unknown	i
	Y	T	A	V	V	P	L	V	Y	J-chain 102-110	i
	Y	T	N	P	Q	F	N	V	Y	Unknown	i
	E	T	X	X	P	D	W	S	Y	Unknown	i
	F	T	D	V	N	S	X	X	R	Unknown	i
	S	S	E	Q	T	F	M	Y	Y	Ornithine decarboxylase 309-317	b
	S	T	E	P	V	N	I	L	Y	Unknown	b
	G	T	D	P	G	V	L	I	Y	Unknown	b
	S	T	E	P	P	M	L	N	Y	Unknown	b
	S	L	E	P	Q	R	T	Q	Y	Unknown	b
	F	T	E	V	S	I	R	K	Y	Unknown	b
	K	F	D	P	V	N	L	V	Y	Unknown	b
	A	V	D	P	G	M	Y	S		Unknown	b
	F	G	S	G	A	R	D	X	Y	Unknown	b
	Y	X	E	P	Q	F	L	T	Y	Unknown	b
	A	X	I	P	A	F	I	N	Y	Unknown	b
	I	T	E	D	M	G	H	L	K	Unknown	f
	E	T	D	X	X	X	D	R	S	Unknown	i
T-cell epitopes	E	A	D	P	T	G	H	S	Y	MAGE-1 161-169	e, k
	V	S	D	G	G	P	N	L	Y	Influenza A PB1 591-599	b, f
	C	T	E	L	K	L	S	D	Y	Influenza A NP 44-52	f
	E	V	D	P	I	G	H	L	Y	MAGE-3	g, h

References:

- a: Falk et al. 1994 c; b: Di Brino et al. 1993 b; c: Sette et al. 1994; d: Engelhard 1994; e: Traversari et al. 1992; f: DiBrino et al. 1994; g: Gaugler et al. 1994; h: Celis et al. 1994; i: Kubo et al. 1994; k: Van der Bruggen et al. 1991

Table 2 (Continued)
B HLA-A*0201

[illegible]

* Class I ligands allocated to A2 by motif. + Also a T-cell epitope

References:

a: Falk et al. 1991 b; b: Hunt et al. 1992; c: Henderson et al. 1992; d: Wei and Cresswell 1992; e: Henderson et al. 1993; f: Wölfel et al. 1994; g: Robbins et al. 1994; h: Brichard et al. 1993; i: Engelhard et al. 1993; j: Walker et al. 1989; k: Gotch et al. 1988; l: Harris et al. 1993; m: Nayersina et al. 1993; n: Bertoletti et al. 1993, 1994; o: Utz et al. 1992; p: Lee et al. 1993; q: Robbins et al. 1989; r: Chisari and co-workers, personal comm.; s: Shirai et al. 1994; t: Tarpey et al. 1994; u: Cox et al. 1994; v: Kawakami et al. 1994 b; w: Coulie et al. 1994; x: Kawakami et al. 1994 a; c; v: Falk et al. 1994 a; z: Bednarek et al. 1991

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues	V					I			L		a
	L					V					
	I					L					
	M					A					
Other preferred residues	Q	Y	G	Y	T		Q	K			
		P	E	V							
		F	D	L							
		I	K	I							
			N								

a: Röttschke et al. 1992

[illegible]

Referências:
a: DiBrino et al. 1993 a; b: Maier et al. 1994; c: Takahashi et al. 1991; d: Koenig et al. 1990; e: Venet and Walker 1993; f: DiBrino et al. 1993 b;
g: Kubo et al. 1994

Table 2 (Continued)
E HLA-A*1101

	Position											Source	Ref.
	1	2	3	4	5	6	7	8	9	10	11		
Anchor or auxiliary anchor residues		V I F Y	M L F Y I A				L I Y V F		K	K	K		a, b, c
Other preferred residues	A	T	N D E Q	P G D E K	P I F V M	I V M		R K N E Q	R D	R	R		
Examples for ligands	A A A G G Y A S K R G A A R V	<u>V</u> <u>V</u> S Q V F T T V V T S A A V	<u>M</u> <u>I</u> E Y D A Y M M F D M E	K L D G P A G Y N N V T K X D Q	P P K N P H N G S L P V L T A D A	E P A P H G S S V L F X T V V	A L K L E I I I F X K K V E	E S L N K F E V E Y L V S	K P K R S R F K K K K M	R Y K S R L R K K K K V	K F K K K K K K K K K	Unknown HSB 66 EST 18-29 Thymosin β -10 11-20 Cattle metalloproteinase 19-27 Ribosomal protein S19 93-101 Elongation factor 2 265-275 Prohibitin (rat) 229-240 Unknown (also presented by A33) Ribosomal protein S6 107-115 Ribosomal protein L7A 25-33 Ribosomal protein S3 54-62 Unknown Thymosin β -10 11-19 Unknown Unknown	b b b b b b, c a, b c c c c c c
T-cell epitope	I	<u>V</u>	T	D	F	S	<u>V</u>	I	K			EBNA 4 416-424	a, d

References:

a: Zhang et al. 1993; b: Falk et al. 1994; c: Kubo et al. 1994; d: Gavioli et al. 1993

F HLA-A24

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Y			I V	F			I L F		a
Other preferred residues			N E L M P G	D P			Q N	E K			
Examples for ligands	K Y A V	Y Y Y Y	P E V X	E E H K	N Q M H	F H V P	F P T V	L E H S	L L F X	Protein phosphatase 1 113-121 NK/T-cell activation protein 107-115 Unknown Unknown	b b b b
T-cell epitope	R	Y	L	K	D	Q	Q	L	L	HIV gp 41 583-591	c

References:

a: Maier et al. 1994; b: Kubo et al. 1994; c: Dai et al. 1992

Table 2 (Continued)
G HLA-A*3101

	Position									Comments	Ref.		
	1	2	3	4	5	6	7	8	9				
Anchor or auxiliary anchor residues		L V Y F	F L Y W			L F V I			R		a		
Other preferred residues	K R	T Q	K N	P D E G S V T	P I V F L Y W	T N D E R	N V D F T H L Y	L R N Q		P1 deduced from individual ligands			
										Source			
Examples for ligands	L Q R K K R	Q Q G V I Y	F L Y F M M	P Y R G P D K D	V W S P W A	G S R I N W	R H F H Y N T	V P R E R Y	H R R R S R	Histon H2 a 23-32 Ribosomal protein S29 (rat) 3-11 CCAAT-binding transcription factor 240-248 [GlcNAc]-P-transferase 371-379 Unknown Lamin B2	a a a a a a		
T-cell epitope	S	T	L	P	E	T	T	V	V	R	R	Hepatitis B cAg 141-151	b

References:

a: Falk et al. 1994 c; b: Missale et al. 1993

H HLA-A*3302

	Position									Comments	Ref.
	1	<u>2</u>	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		A I L F Y V							R		a
Preferred residues	D E	T	L K	P	P	I L F				P1 deduced from individual ligands	
Other possible residues	M		Q W E N	R D E G S H P	R I F P V L W	R D H Y T S	H Y V T S	Q N E M			
										Source	
Examples for ligands	D E T D E T	M S <u>Y</u> <u>Y</u> I I	A G Y I M M	A P G H K P	Q S S I W K D	I I S R N I	T V V I R Q L	Q H R Q E L	R R R R R A R R	HLA class I α -chain 161-169 Actin 364-372 Unknown Human cDNA HSB15F102 65-74 Unknown Histon 3.1/3.3 118-129	a a a a a a
T-cell epitope	I	V	G	L	N	K	I	V	R	HIV p24 gag 267-275	b, c

References:

a: Falk et al. 1994 c; b: Buseyne et al. 1993; c: Buseyne and Riviere 1993

Table 2 (Continued)
I HLA-A68.1

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor residues		V T							R K		a
Examples for ligands	A	V	A	A	V	A	A	R	R	Unknown	a
	E	V	A	P	P	E	Y	H	R	Unknown	a
	E	V	A	P	P	E	Y	H	R	Unknown	a
	D	V	F	R	D	P	A	L	K	Homologous ribosomal 60S	a
	K	T	G	G	P	I	Y	K	R*	Influenza NP 91-99	a, b
	E	V	I	L	I	D	P	F	H	Unknown	a
	T	V	F	D	A	K	R	L	I	HSP 70B / HSC70 66-76	a
	X	V	L	K	X	I	A	K	R*	Unknown	d
	P	V	K	Q	V	V	Y	H	R*	Unknown	d
	E	S	G	P	S	I	V	H	R	β -Actin 364-373	d
	T	T	X	T	T	T	N	A	R*	Unknown	d
	D	T	T	P	T	X	X	R*		Unknown	d
T-cell epitopes	S	T	L	P	E	T	T	V	V	Hepatitis B cAg 141-151	c

* Class I ligands allocated to A68.1 by motif +Also a T-cell epitope

References:

a: Guo et al. 1992; b: Silver et al. 1992; c: Missale et al. 1993; d: Harris et al. 1993

Table 3 HLA-B motifs
A HLA-B7

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		P	R						L F		a, b
Other preferred residues				D G	D P	F T	L				
Also detected	A H S		D E Q K Y F M N A	E H L K S T P	I V L I	R L I	V				
Examples for ligands	A	P	R	T	V	A	L	T	A	HLA-DP signal sequence 9-17	a
	A	P	R	T	V	A	L	T	A	HLA-DP signal sequence 9-18	a
	A	P	R	A	X	X	X	X	X	Unknown	a
	A	P	R	X	P	X	T	G	X	Unknown	a
	A	P	R	A	S	R	P	S	X	Unknown	a
	A	P	R	T	L	V	L	L	L	HLA-A2.1 signal sequence 5-13	a
	M	P	R	G	V	V	V	T	X	Unknown	a
	S	P	R	Y	I	F	T	M	L	Topoisomerase II 801-809	a
	A	P	A	P	T	V	A	V	X	Unknown	a
	R	P	S	G	P	G	P	E	X	Unknown	a
	L	V	M	A	P	R	T	V	L	HLA-B7 signal sequence 2-10	a
	R	V	M	A	P	R	A	X	X	Unknown	a
	A	P	R	A	F	X	P	X	P	Unknown	a
	A	A	S	K	E	R	S	G	V	Histone H1 49-59	a
	A	P	R	S	N	G	M	V	X	Unknown	c
	A	P	R	Q	P	G	X	M	A	Unknown	c
	A	P	A	P	P	P	K	p	M	Ribosomal S26 protein 107-115	c
	A	P	Y	G	G	P	X	A	X	Unknown	c
T-cell epitope	T	P	G	P	G	V	R	Y	P	HIV-1 nef 128-137	d

References:

a: Huczko et al. 1993; b: Maier et al. 1994; c: Engelhard 1994; d: Culmann et al. 1991

[illegible]

a: Malcherek et al. 1993; b: Sutton et al. 1993; c: Burrows et al. 1990; d: DiBrino et al. 1994; e: Phillips et al. 1989; f: Achour et al. 1990

Table 3 (Continued)
C HLA-B*2702

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor residues	R								F Y I L W		a
Other preferred residues	K		F L X	G P K E D V M Q T S	I K E Y R D H E Q	I V Y T F	Y L V D E R	K V D E R			
Examples for ligands	S G R K K K G G	R R R R R R R	D L F Y K G F	K T V K A I G K	T K N S A L V L	I H V I Y T G I	I T V V A L N V	M K P K D K R L	W F T Y F Y Y	HGNBPβ-subunit 35-43 Rat ribosomal protein L36 36-44 Human fau protein 114-123 HFPS 191-199 Cytochrome C oxidase 42-50 Actin 63-71 Unknown Unknown	a a a a a a a a

References:

a: Rötzschke et al. 1994

[illegible]

* B*2704-restricted

References:

- a: Jardetzky et al. 1991; b: Röttschke et al. 1994; c: Shepherd et al. 1993; d: Huet et al. 1990; e: Brooks et al. 1993; f: van Binnendijk et al. 1993; g: Busevne et al. 1993; h: Cerrone et al. 1991; i: Frumentó et al. 1993

Table 3 (Continued)
E HLA-B*3501

	Position										Source	Ref.
	1	2	3	4	5	6	7	8	9	10		
Anchor or auxiliary anchor residues		P							Y F M L I	Y		a, b
Other preferred residues	M	A V Y R D	I L F V M E T Y N	K D E G P	D I V T E G L M	I Q N V L M	V N E Q T	E Q V				
T-cell epitopes	K K K A	P S P S	K K N R	D D D C	E E K W	L L S V	D D L A	Y Y Y M			P. falciparum CSP 368-375 P. falciparum CSP 368-375 P. falciparum LS 1850-1857 HCV E1 235-242	a a a c

References:

a: Hill et al. 1992; b: Falk et al. 1993b; c: Koziel et al. 1992

F HLA-B*3701

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		D E			V I			F M L	I L		a
Other preferred residues	K Q	H P G S L			T R A D G H M		Q K Y L	T E N D Q G H			
T-cell epitope	E	D	L	R	V	L	S	F	I	Influenza NP 339-347	b

References:

a: Falk et al. 1993b; b: Townsend et al. 1986

G HLA-B*3801

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		H	D						F		a
			E						L		
Other preferred residues	I	F	I	G	M	V	Y	K	I		
		P	A	E	T	I	V	Y			
		W	S	P	V	T	N	N			
		Y	N	L	A	K		R			
			M	V	E	R		T			
			V		G	N					
					L	H					
					K						
					S						
Examples for ligands	E	H	A	G	V	I	S	V	L	Unknown	a
	T	H	D	E	L	E	D	K	L	Unknown	a
	Q	Y	D	E	A	V	A	Q	F	Histone binding protein 627-635	a
	Y	P	D	P	A	N	G	K	F	Elongation factor 2 265-273	a
	S	H	I	G	D	A	V	V		Cyclin 152-159	a
	Y	H	E	D	I	H	T	Y	L	Cyclin A 178-186	a
	T	F	D	V	A	P	S	R	L	Pm5 protein 270-278	a

References:

a: Falk et al. 1995 b

H HLA-B*39011

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		R				I			L		a
		H				V					
						L					
Other preferred residues			A	D	V	N	N	S	V		
			D	E	Y		Y	K	I		
			I	G	I		F	R	M		
			L	P	L			E			
			F	K	F			T			
			V		T						
			M		G						
			S		K						
			T		N						
			Y		P						
Examples for ligands	S	H	I	G	D	A	V	V		Cyclin 152-159	a
	I	H	E	P	E	P	H	I		CKShs1 protein 59-66	a
	S	R	D	K	T	I	I	M		GBLP 35-42	a

References:

a: Falk et al. 1995 b

Table 3 (Continued)
I HLA-B*3902

	Position									Ref.
	1	2	3	4	<u>5</u>	6	7	8	9	
Anchor or auxiliary anchor residues		K Q			I L F V				L	a
Other preferred residues	K A	A I F V N L T Y E H S	G P	N E G P Q S T	V Y T H F I M P R	V L T Y N D H	T S R	F M		

References:

a: Falk et al. 1995 b

K HLA-B40*

	Position											Source	Ref.	
	1	2	3	4	5	6	7	8	9	10	11			
Anchor or auxiliary anchor residues		E	F I V						L W M A				a	
Examples for ligands	T	E	F	P	K	E	R	H	L	R	L	Unknown	a	
	G	E	F	P	N	K	N	X	L			Unknown	a	
	G	E	F	P	N	K	N	X	L	Y	A	Unknown	a	
	G	E	F	P	G	K	I	F	L	Y	A	Unknown	a	
	W	E	F	L	Q	P	I	L	L			Unknown	a	
	G	E	F	I	P	G	N	D	L	H	R	Unknown	a	
	G	E	F	P	P	X	D	N	W			Unknown	a	
	E	E	F	Y	V	D	L	E	R			HLA-DQ α 33-41	a	
	N	E	F	P	D	I	D	I	R			Unknown	a	
	A	E	F	P	K	X	E	A	R			Unknown	a	
	A	E	I	G	E	V	I	V	L	W	X	W	Unknown	a
	A	E	I	P	G	E	I	A	L			Unknown	a	
	G	E	I	L	D	V	F	D	A			IRE-BP 695-703	a	
	F	E	I	P	X	L	D	V	A			Unknown	a	
	D	E	V	T	P	Q	P	Q	L	V			Unknown	a
	K	E	V	G	V	D	V	A	L	Y	A		Unknown	a
K	E	S	T	L	H	L	V	L				Ubiquitin 63-71	a	
G	E	V	D	V	E	Q	H	T				Cyclin B 313-321	a	
H	E	E	T	P	P	T	T	S				c-myc 241-249	a	

* Motif and ligands deduced by exclusion: Class I ligands from a c-myc transfected B-cell line expressing A2, A68, and B40 were sequenced. Those not containing an A2 or A68 motif were thought to contain B40 ligands.

References:

a: Harris et al. 1993

Table 3 (Continued)
L HLA-B*4402

	Position										Ref.
	1	2	3	4	5	6	7	8	9	10	
Anchor or auxiliary anchor residues		E							F Y	F Y	a
Preferred residues	A S		M I L D		I	V	Y				
Others	D		N	P R K							

References:

a: Fleischhauer et al. 1994

M HLA-B*4403

	Position										Source	Ref.
	1	2	3	4	5	6	7	8	9	10		
Anchor or auxiliary anchor residues		E							Y F	Y F		a
Preferred residues	A S		M I L V D									
Others			N	P R K	I V K		Y F					
Examples for ligands	A A	E E	D M	K G	E K	N G	Y S	K F	K K	F Y	HSP 90 427-436 Elongation factor 2 48-57	a a
B*440x-restricted T-cell epitope	E	E	N	L	L	D	F	V	R	F	EBNA 6 130-139	b

References:

a: Fleischhauer et al. 1994; b: Khanna et al. 1992

Table 3 (Continued)
N HLA-B*5101

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		A P G							F I		a
Other preferred residues	I L V Y D	W F	I L M F W Y V E H D R N	G V I K E D S	V T G A I S	N I L K Q	K Q R E	T	W M V L		
Examples for ligands	Y D T d l	P A G Y P	F H Y Y P	K I L A E	P Y L L V	P L N N N	K N T H R	V H T T Q	I I V L L	UBC5, yeast 61-68 Thymidylate synthase 253-261 GBLP 192-200 Unknown Unknown	a a a a a

References:

a: Falk et al. 1995 a

O HLA-B*5102

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		P A G	Y						I V		a
Other preferred residues			F V L I	G E K L T Q R N H	V Q N G T	I N Q T	R E Q K	T R Y			
Examples for ligands	Y Y L L T F F M	A P P P G P P	Y F P Y Y S W	D K G D E I F K	G P R T N G I K G	K P I I T K V w	D I I V D V G	Y V K T Y K K	I X v V I I R I V	MHC I α chain 140-148 UBC5, yeast 61-68 Unknown CDC25 homol. 560-567 GBLP 192-200 MHC I α chain 140-148 Ribosomal protein S7/S8A 135-144 Elongation factor 1a 208-216	a a a a a a a a

References:

a: Falk et al. 1995 a

Table 3 (Continued)
P HLA-B*5103

	Position									Comments	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		A P G	Y						V I F	Anchor at 9 deduced from individual ligands	a
Other preferred residues	T V D	F W	F D L	E L N R G Q T V	G A V N Q M R	I K T	V M				
Source											
Examples for ligands	T	G	Y	L	N	T	V	T	V	GBLP 192-199	a
	D	A	H	I	Y	L	N	H	I	Thymidilate synthase 253-261	a
	Y	F	D	d	t	L	E	D	F	Unknown	a

References:

a: Falk et al. 1995a

Q HLA-B*5201

	Position									Comments	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Q	F Y W		L I V			I V	I V	C-terminal anchor at 8 or 9	a
Other preferred residues	V L I	M F P	I L P D K	L I V P K E A	M F A T G	K N L T S	K E Y	M F	M F		
Source											
Examples for ligands	T	G	Y	L	N	T	V	T	V	GBLP 192-200	a
	G	Q	F	K	T	Y	A	I		Ribos. prot. S21 60-67	a
	H	S	T	I	M	P	R	L		P1-CDC21 259-266	a
	G	F	Y	P	G	S	I	E	V	MHC II β chain 150-158	a
	V	Q	I	F	G	N	K	M		RBAP-2 266-273	a
	Y	P	D	P	A	N	G	K	F	Elongation factor 2 265-273	a
	L	Q	F	P	V	G	R	I		Histone 2a Z 25-32	a
	H	M	Y	I	F	L	H	T	V	Unknown	a

References:

a: Falk et al. 1995a

Table 3 (Continued)
R HLA-B53

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor residues	P										a
T-cell epitope	K	P	I	V	Q	Y	D	N	F	P. falciparum LSA-1 1786-1794	a

References:

a: Hill et al. 1992

S HLA-B*5801

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		A S T		P E K	V I L M F				F W		a
Other preferred residues	K R I	G	G T I L V F Y N Q	D Q R	A D N T Y W Q	I V L F	L Y M N	N R K T	Y		
Examples for ligands	K A I R I I K V g	A G t T S S t T A	G D T S D D S V	Q R K G S S e P N	V T A K D N V L V	V F I V D P V T V	T Q S F L T E M	I K R Q H S L T L f	W W F F S T W f	Lamin C 490-498 MHC class I 260-268 Unknown Ribosomal protein L30 23-31 Cytochrome C oxidase 154-163 Unknown Unknown MHC class IIβ 209-217 Glucose transporter 5 322-330	a a a a a a a a

References:

a: Falk et al. 1995c

Table 3 (Continued)
T HLA-B60 (B*40012)

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		E					I V		L		a
Other preferred residues			A V I L M F S D N	P K D G N Q T	L I V D T P G Q	K N P V I D R Q	L Y M	K R Q			
Examples for ligands	K H Y S I	E E E E E	S A I S V	T T H P D	L L D G P D	H R G V D	L c M V T	V w N V K	L A L L E	Ubiquitin 63-71 MHC class I 221-230 HSHMO2C05 Signal peptidase 45-54 Ribosomal protein S17 95-105	a a a a a

References:

a: Falk et al. 1995 c

U HLA-B61 (B*4006)

	Position									Comments	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		E	F I L V Y W			I			V		a
Other preferred residues	G R	P	M T	E G P S N D K A R N Q	V I L M D G V F N S K	N	Y V L W I T R D Q G	K S	A P	P1 deduced from individual ligands	
Examples for ligands	G E G R R G G R	E E E E E E E	F F F R I F H M	G Q V R I S G I P	G F D D I L L F	F I L N T i F	G K Y Y N Y i A	S K V V A K R D	V A V V V V i	IEF (mRNA) 9306 127-135 Associated-microfibril. protein 72-80 Ribosomal protein S21 6-13 Ribosomal protein S17 77-84 Ribonucl. reductase 290-297 Ribosomal protein S15 116-123 Unknown Unknown	a a a a a a a

References:

a: Falk et al. 1995 c

Table 3 (Continued)
V HLA-B62 (B*1501)

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Q L			I V				F Y		a
Other preferred residues	I	M V	K A N F P Y H R	P E G D	G L F T	V T G I	V T L I	Y V T			
Examples for ligands	V Y G K I S G V	L L Q I Q Q Q	K G R K P F R G	P E K S G G K P V	G F G R G G P V	M S A V G S A G	V I G K F S T L	V T S V V L Y	F Y Y Y Y Y	Elongation factor 1 α 271-280 Ribosomal protein S15 114-122 Ribosomal protein L8 (rat) 7-15 Ribosomal protein L27 66-74 Unknown Unknown Ribosomal protein L28 (rat) 68-76 Collagen α 1 1106-1112	a a a a a a a
T-cell epitopes	I	L	G	N	K	I	V	R	M Y	HIV gag 267-276	b

References:

a: Falk et al. 1995 c; b: Buseyne et al. 1993

W HLA-B*7801

	Position								Comments	Ref.
	1	2	3	4	5	6	7	8		
Anchor or auxiliary anchor residues		P A G				I L F V		A	This motif is only partial; the C-terminal anchor has not been determined	a
Other preferred residues			Y D W	F D G L V S Q R N	D G V N R Q S T		A V N K Q E	K S		

References:

a: Falk et al. 1995 a

Table 4 HLA-C motifs
A HLA-Cw*0301

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues			V I Y L M	P		F Y			L F M I		a
Other preferred residues		A R	E N	E R	N	M	Q K S M	T			
T-cell epitopes	H or Q	Q M	A V	I H	S Q	P A	R I	T S	L P	HIV gag 144-152 HIV gag 141-152	b

References:

a: Falk et al. 1993a; b: Littau et al. 1991

B HLA-Cw*0401

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Y P F				V I L			L F M		a
Other preferred residues			D H	D E P	A H M T R		A	K S H			
T-cell epitope	S	F	N	C	G	G	E	F	F	HIV-1 gp 120 380-388	b

References:

a: Falk et al. 1993a; b: Johnson et al. 1993

C HLA-Cw*0602

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues					I L F M	V I L			L I V Y		a
Other preferred residues	I F K Y	P R	P I G F Y K N A	P E D Q L	K	A T S	R K Q N	Y E Q N R G T S K			
Examples for ligands	Y V F X	Q R A Q	F H F r	T D p T	G G l P	I G l k	K N q A	K V R g	Y L V I	Unknown Unknown Unknown Unknown	a a a a

References:

a: Falk et al. 1993a

Table 4 (Continued)
D HLA-Cw*0702

	Position									Source	Ref.
	1	2	3	4	5	6	7	8	9		
Anchor or auxiliary anchor residues		Y P			V Y I L F M	V I L M			Y F L		a
Other preferred residues		R D	P G A	D E V Q P S G	T	A R	Y M N R V F E	E A F D K			
Examples for ligands	K R N I I N	<u>Y</u> <u>Y</u> K <u>Y</u> R <u>Y</u>	F R A P K G	D P D q P G	E G <u>V</u> n <u>Y</u> G	H T I v I N	Y V L i w Y	E A K L E S	Y L Y Y S	CKS-2 11-19 Histone H3.3 40-48 Protein synthesis factor eIF-4C 87-95 Unknown Glutamyl-tRNA synthetase 343-351 Homologous hnRNP A2 or B1 (S11 = N) 277-288 Unknown Unknown	a a a a a a a a
	F X	<u>Y</u> M	P P	P P	y I	l <u>I</u>	Y d		G		

References:

a: Falk et al. 1993a

Table 5 Processing motif for all MHC class II ligands

	Absolute position																	Ref.
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	
	P																	a, b, c

References:

a: Falk et al. 1994b; b: Kropshofer et al. 1993; c: Malcherek et al. 1993

Table 6 Human MHC class II motifs
A HLA-DRB1*0101

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor residues		Y,V, L,F, I,A M,W			L,A I,V M,N Q		A,G S,T P			L,A I,V N,F Y		a, b, c	
Examples for ligands	VGSD	W	R	F	L	R	G	Y	H	Q	YA	HLA-A2 103-117	c
	VGSD	W	R	F	L	R	G	Y	H	Q	YAYDG	HLA-A2 103-120	c
	VGSD	W	R	F	L	R	G	Y	H	Q	Y	HLA-A2 103-116	c
	GSD	W	R	F	L	R	G	Y	H	Q	YA	HLA-A2 104-117	c
	LPKPPKPVSK	M	R	M	A	T	P	L	L	M	QALPM	Invariant chain 97-120	c
	IPAD	L	R	I	I	S	A	N	G	C	K	Na ⁺ -K ⁺ -ATPase 199-216	c
	RVE	Y	H	F	L	S	P	Y	V	S	PKESP	Transferrin receptor 680-696	c
	YKHT	L	N	Q	I	D	S	V	K	V	WPRRPT	Cattle fetuin 56-74	c
	AJLE	F	R	A	M	A	Q	F	S	R	KTD	Unknown	d
PK	Y	V	K	Q	N	T	L	K	L	AT*	Influenza HA 306-318	e	

* Alignment determined by structural analysis

References:

a: Hammer et al. 1992; b: Falk et al. 1994b; c: Chicz et al. 1992; d: Kropshofer et al. 1992; e: Stern et al. 1994

Table 6 (Continued)
B HLA-DRB1*0301 (DR17)

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or auxiliary anchor residues		L,I F,M V			D		K,R E,Q N			Y,L F		a, b, c	
Examples for ligands	ISNQ	L	T	L	D	S	N	T	K	Y	FHKLN	Apolipoprotein B 2877-2894	a
	ISNQ	L	T	L	D	S	N	T	K	Y	FHKL	Apolipoprotein B 2877-2893	a
	ISNQ	L	T	L	D	S	N	T	K	Y	FHK	Apolipoprotein B 2877-2892	a
	VDT	F	L	E	D	V	K	N	L	Y	HSEA	α 1-Antitrypsin 149-164	a
	KPRA	I	V	V	D	P	V	H	G	F	MY	LDL-Receptor 518-532	a
	KQT	I	S	P	D	Y	R	N	M	I		IgG2a, Membrane domain	a
	YPD	F	I	M	D	P	K	E	K	D	KV	Unknown	a
	NIQ	L	I	N	D	Q	E	V	A	R	FD	Unknown	a
	LLS	F	V	R	D	L	N	Q	Y	R	ADI	Transferrin receptor 618-632	a
	LPKPPKPVSK	M	R	M	A	T	P	L				Invariant chain 97-113	d, e, f
	LPKPPKPVSK	M	R	M	A	T	P	L	L	M	QALP	Invariant chain 97-119	d, e, f
	LPKPPKPVSK	M	R	M	A	T	P	L	L	M	QALPM	Invariant chain 97-120	d, e, f
	PKPPKPVSK	M	R	M	A	T	P	L				Invariant chain 98-113	d, e, f
	PKPPKPVSK	M	R	M	A	T	P	L	L	M	QA	Invariant chain 98-117	d, e, f
	KPPKPVSK	M	R	M	A	T	P	L	L	M	Q	Invariant chain 99-116	d, e, f
	KPPKPVSK	M	R	M	A	T	P	L	L	M	QALPM	Invariant chain 99-119	d, e, f
	VDDTQF	V	R	F	D	S	D	A	A	S	Q	HLA-A30 28-?	e
	ATKYGN	M	T	E	D	H	V	M	H	L	LQNA	Invariant chain 131-149	e
	VFL	L	L	A	D	K	V	P	E	T	SLS	ACh receptor 289-304	e
	LNK	I	L	L	D	E	Q	A	Q	W	K	ICAM-2 64-76	e
	GPPKLD	I	R	K	E	E	K	Q	I	M	IDIFH	IFN- γ receptor 128-147	e
	GPPKLD	I	R	K	E	E	K	Q	I	M	IDIFHP	IFN- γ receptor 128-148	e
	GKFA	I	R	P	D	K	K	S	N	P	IIRTV	Cyt-b5 155-172	e
	YAN	I	L	L	D	R	R	V	P	Q	TDMTF	Apolipoprotein B 1207-1224	e
	NLF	L	K	S	D	G	R	I	K	Y	TLNKNLSL	Apolipoprotein B 1276-1295	e
	IPDNLF	L	K	S	D	G	R	I	K	Y	TLNKN	Apolipoprotein B 1273-1292	e
	IPDNLF	L	K	S	D	G	R	I	K	Y	TLNK	Apolipoprotein B 1273-1291	e
	IPDNLF	L	K	S	D	G	R	I	K	Y	TLN	Apolipoprotein B 1273-1290	a, e
	NLF	L	K	S	D	G	R	I	K	Y	TL	Apolipoprotein B 1273-1289	e
	NLF	L	K	S	D	G	R	I	K	Y	TLNK	Apolipoprotein B 1276-1291	e
	NLF	L	K	S	D	G	R	I	K	Y	TLN	Apolipoprotein B 1276-1290	e
	VTT	L	N	S	D	L	K	Y	N	A	LDLTN	Apolipoprotein B 1294-1810	e
	V	G	S	D	W	R	F	L	R		GYHQYA	HLA-A2 103-117	e

References:

a: Malcherek et al. 1993; b: Geluk et al. 1994; c: Geluk et al. 1992; d: Riberdy et al. 1992; e: Chicz et al. 1993; f: Sette et al. 1992

Table 6 (Continued)
C HLA-DRB1*0401 (DR4Dw4)

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		F,Y W,I L,V M			F,W I,L V,A D,E no R,K		N,S T,Q H,R	pol.* chg.* ali.*		pol.* ali.* K		a, b, c, d	
Examples for ligands	VDDTQ	F	V	R	F	D	S	D	A	A	SQRMPEP	HLA-A2 33-47	a
		F	V	R	F	D	S	D	A	A	SQRM	HLA-A2 28-45	a
		F	V	R	F	D	S	D	A	A	SQRM	HLA-A2 33-45	a
	VDDTQ	F	V	R	F	D	S	D	A	A	SPRGEP...	HLA-C 28-?	a
	DGKD	Y	I	A	L	N	E	D	L	S	S	HLA-B44 143-156	a
	LSS	W	T	A	A	D	T	A	A	Q	ITQ	HLA-B44 154-168	a
	LSS	W	T	A	A	D	T	A	A	Q	IT	HLA-B44 154-167	a
	IY	F	R	N	Q	K	G	S	H	S	GLQPTGFL	HLA-DR4β 252-270	a
	DVA	F	V	K	D	Q	T	V	I	Q	NTD	Cattle transferrin 68-82	a
	YDHN	F	V	K	A	I	N	A	I	Q	KSW	Cathepsin C 170-185	a
	KHKV	Y	A	C	E	V	T	H	Q	G	...	Igκ chain C region 80-?	a
	HKV	Y	A	C	E	V	T	H	Q	G	L...	Igκ chain C region 81-?	a
	DGP	F	R	I	I	T	V	P	A	A	LDY	Unknown	a
	TGN	Y	R	I	E	S	V	L	S	S		Sphingolipid activator protein 3 165-176	a
	GERA	M	T	K	D	N	N	L	L	G	...	HSC 70 445-?	a
	XXX	Y	E	X	A	L	S	L	P	S	K...	Unknown	a
	GSLF	V	Y	N	I	T	T	N	K	Y	KAFLKQ	VLA-4 229-247	e
	SPEDF	V	Y	Q	F	K	G	M	C	Y	F	HLA-DQβ 3.2 chain 24-38	c
	AAPYEKEVP	L	S	A	L	T	N	I	L	S	AQL	PAI-1 261-281	e
	GVYF	Y	L	Q	W	G	R	S	T	L	VSVS	Ig heavy chain 121-?	e
AEALERM	F	L	S	F	P	T	T	K	T		Cattle hemoglobin 26-41	e	
LRS	W	T	A	A	D	T	A	A	Q	ITQRKWEAA	HLA-Cw9 130-150	e	
DLSS	W	T	A	A	D	T	A	A	Q	ITQRKWEAA	HLA-Bw62 129-150	e	
APSP	L	P	E	T	T	E	N	V	V	CALG	HLA-DRα chain 182-198	e	

* pol.: Polar; chg.: charged; ali.: aliphatic

References:

a: Friede and co-workers, submitted; b: Seitz et al. 1993; c: Hammer et al. 1993; d: Hill et al. 1994; e: Chiczy et al. 1993

D HLA-DRB1*0402 (DR4Dw10)

		Relative position									Source		Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		V,I L,M			Y,F W,I L,M R,N no D,E		N,Q S,T K	R,K H,N Q,P; rare D,E		pol.* ali.* H			a
Examples for ligands	GPDGR	L	L	R	G	H	N	Q	F	A	YDGKD	HLA-B38 128-146	a
	GR	L	L	R	G	H	N	Q	F	A	YDGK	HLA-B38 131-145	a
	I	I	K	G	V	R	K	S	N	A	AERRG	HLA-DRα 238-252	a
		I	Y	F	R	N	Q	K	G	H	SGLQPTGFLS	DR4β 248-266	a
				F	R	N	Q	K	G	H	SGLQP	DR4β 250-261	a
	F	I	Y	F	R	N	Q	K	G	H	SGLQPTGFLS	DR4β 249-266	a
		Y	V	R	F	D	S	D	V	G	EY	DR4Dw10β 37-47	a
	LPKPPKPVSK	M	R	M	A	T	P	L	L	Q		Invariant chain 97-?	a
	FDQK	I	V	E	W	D	S	R	K	S	KYFE	BLAST-1 62-78	a
	DQK	I	V	E	W	D	S	R	K	S	KYF	BLAST-1 63-77	a
	IKI	I	S	K	I	E	N	H	E	G	VRR	Pyruvate kinase 264-278	a
	IKI	I	S	K	I	E	N	H	E	G	VR	Pyruvate-kinase 264-277	a
	FGR	I	G	R	L	V	T	R	A	A	FNSG	GAPDH 11-25	a
	FGR	I	G	R	L	V	T	R	A	A	FN	GAPDH 11-23	a
	GFGR	I	G	R	L	V	T	R	A	A	FNSG	GAPDH 10-25	a
	CNE	I	I	N	W	L	D	K	N	Q		HSC 70 574-585	a
QPD	L	R	Y	L	F	L	N	G	N		Leucine-rich α2-glyco-protein 200-211	a	

References:

a: Friede and co-workers, submitted

Table 6 (Continued)

E HLA-DRB1*0404 (DR4Dw14)

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		V,I L,M			F,Y W,I L,V M,A D,E no R,K		N,T S,Q R	pol.* chg.* ali.*		pol.* ali.* K		a	
Examples for ligands	GSMS	M	R	Y	F	H	T	A	M	S	RPGRGE	HLA-B60 1-?	a
	SHS	M	R	Y	F	H	T	A	M	S	RPGRGE	HLA-B60 2-?	a
	YDNS	L	K	I	I	S	N	A	S	C	TTN	GAPDH 139-154	a

* pol.: Polar; chg.: charged; ali.: aliphatic

References:

a: Friede and co-workers, submitted

F HLA-DRB1*0405 (DR4Dw15)

		Relative position											Source	Ref.
		1	2	3	4	5	6	7	8	9				
Anchor or preferred residues		F,Y W,V I,L M			V,I L,M D,E		N,S T,Q K,D	pol.* chg.* ali.*		D,E Q				a
Examples for ligands	YPTQRRAR	Y	Q	W	V	R	C	N	P	D	SNS	PGSG 1-19	a	
	QRAR	Y	Q	W	V	R	C	N	P	D	SNS	PGSG 4-19	a	
	RAR	Y	Q	W	V	R	C	N	P	D	SNS	PGSG 5-19	a	
	KPPQ	Y	I	A	V	H	V	V	P	D	Q	MIF 32-45	a	
	FRE	F	K	L	S	K	V	W	R	D	QH	Transferrin receptor 173-186	a	
	FRE	F	K	L	S	K	V	W	R	D	Q	Transferrin receptor 173-185	a	
	RE	F	K	L	S	K	V	W	R	D	QH	Transferrin receptor 174-186	a	
	RE	F	K	L	S	K	V	W	R	D	Q	Transferrin receptor 174-185	a	
	VEPDH	Y	V	V	V	G	A	Q	R	D	A	Transferrin receptor 397-411	a	
	EPDH	Y	V	V	V	G	A	Q	R	D	A	Transferrin receptor 398-411	a	
	THY	Y	A	V	A	V	V	K	K	D	TDFK	Transferrin 92-107	a	
	KELK	I	D	I	I	P	N	P	Q	E	R	Hsp 90-beta 68-81	a	
	YLL	Y	Y	T	E	F	T	P	T	E	KD	β 2-microglobulin 83-96	a	
	LL	Y	Y	T	E	F	T	P	T	E	KDEY	β 2-microglobulin 84-98	a	
	CAIHA KR	V	T	I	M	P	K	D	I	Q	LA...	Histone H3 110-?	a	
	APNT	F	K	T	L	D	S	W	R	D		ras-related protein RAB-7 (rat) 86-98	a	
	VADK	I	Q	L	I	N	N	M	L	D		Phosphoglycerate kinase 216-228	a	
	GSTV	F	D	N	L	P	N	P	E	I	DGDYYGW	Unknown	b	
	XXXQ	Y	I	A	V	H	V	V	P	D	QT	Homol. MIF 32-46	b	
	SDPIL	Y	R	P	V	A	V	A	L	D		PKM2 99-112	b	
		V	P	I	Q	R	A	V	Y	Q	NVVVNPNXD	Unknown	b	
	SPGTGA	Y	Y	V	L	L	N					Unknown	b	
	KPPQ	Y	I	A	V	H	V	V	P	D	QLM	MIF 32-47	c	
	KPPQ	Y	I	A	V	H	V	V	P	D	QL	MIF 32-46	c	
	KPPQ	Y	I	A	V	H	V	V	P	D	Q	MIF 32-45	c	
	DPIL	Y	R	P	V	A	V	A	L	D	TKGPE	PKM2 101-118	c	
	DPIL	Y	R	P	V	A	V	A	L	D	TKGP	PKM2 101-117	c	
	DNPQTHY	Y	A	V	A	V	V	K	K	D	TDFKL	Transferrin 88-108	c	
	DNPQTHY	Y	A	V	A	V	V	K	K	D	TDFK	Transferrin 88-107	c	
	NPQTHY	Y	A	V	A	V	V	K	K	D	TDFKL	Transferrin 89-108	c	
	NPQTHY	Y	A	V	A	V	V	K	K	D	TDFK	Transferrin 89-107	c	
	DNPQTHY	Y	A	V	A	V	V	K	K	D		Transferrin 88-103	c	
THY	Y	A	V	A	V	V	K	K	D	TDF	Transferrin 92-106	c		
LL	Y	Y	T	E	F	T	P	T	E	KDEY	β 2m 84-98	c		
L	Y	Y	T	E	F	T	P	T	E	KD	β 2m 85-26	c		
XXXXKK	V	V	V	Y	L	Q	K	L	D	T	Cathepsin C 58-73	c		
KK	V	V	V	Y	L	Q	K	L	D	TAYD	Cathepsin C 62-76	c		
K	V	V	V	Y	L	Q	K	L	D	TAYD	Cathepsin C 63-76	c		
KP	Y	N	E	A	K	T	X	F	D	KY	Apolipoprotein B-100 3218-3230	c		

* pol.: Polar; chg.: charged; ali.: aliphatic

References:

a: Friede and co-workers, submitted; b: Margue et al., 1994; c: ...

Table 6 (Continued)
G HLA-DRB1*1101

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor residues		W,Y F			M,L V,I		R,K					a, b	
Examples for ligands	IDF	Y	T	S	I	T	R	A	R	F	EE	HSC 70 291-305	b
	CPAG	Y	T	C	N	V	K	A	R	S	CEK	Granulin D 41-56	b
	VNH	F	I	A	E	F	K	R	K	H	KKD	Homol. HSC 70 238-252	b
	VNH	F	I	A	E	F	K	R	K	H	K	Homol. HSC 70 238-250	b
	MR	Y	F	H	T	S	V	S	R	P	GRGEP	HLA-Bw61 5-20	b
	KHKV	Y	A	C	E	V	T	H	Q	G	LS	Homol. Ig κ-chain 190-204	b

References:

a: Hammer et al. 1993; b: Newcomb and Cresswell 1993

H HLA-DRB1*1201

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor residues		I,L F,Y V		L,M N,V A			V,Y F,I N,A			Y,F M,I V		a	
Examples for ligands	GPDGRL	L	R	G	Y	D	Q	F	A	Y	DGK	HLA-B38 104-121	a
	GPDGRL	L	R	G	H	N	Q	Y	A	Y	D	HLA class I 104-119	a
	TGT	I	K	L	L	N	E	N	S	Y	VP	Transferrin receptor 142-155	a
	T	I	K	L	L	N	E	N	S	Y	VPR	Transferrin receptor 144-156	a
	FTGT	I	K	L	L	N	E	N	S	Y	VPR	Transferrin receptor 141-156	a
	DFTGT	I	K	L	L	N	E	N	S	Y	VPR	Transferrin receptor 140-156	a
	SDEK	I	R	M	N	R	V	V	R	N	NLR	Valosin-cont. protein p97 78-93	a
	SSV	I	T	L	N	T	N	V	G	L	YXQT	Homol. to apolipoprotein	a
	EAL	I	H	Q	L	K	I	N	P	Y	VLS	Unknown	a
AHL	F	K	Q	N	K	V	V	H	V	NG	Dihydrolipoamide dehydrogenase 138-152	b	

References:

a: Falk et al. 1994b; b: Falk and co-workers, unpublished

I HLA-DRB1*1501 (DR2b)

		Relative position									Source		Ref.
		1	2	3	4	5	6	7	8	9			
Anchor residues		L,V I			F,Y I			I,L V,M, F					a, b
Examples for ligands	EAEQ	L	R	A	Y	L	D	G	T	G	VE	HLA-A3 152-166	a
		L	E	E	F	G	R	F	A	S	FEAQG	HLA-DRα 45-58	a
	D	V	G	V	Y	R	A	V	T	P	QGRPDA	HLA-DQw6 43-58	a
T-cell epitope	PV	V	H	F	F	K	N	I	V	T		MBP 85-95	b

References:

a: Vogt et al. 1994; b: Wucherpfennig et al. 1994

Table 6 (Continued)
K HLA-DRB5*0101 (DR2a)

		Relative position										Source	Ref.
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		F,Y L,M			Q,V I,M					R,K		a, b	
Examples for ligands	DVG V	Y	R	A	V	T	P	Q	G	R	P	HLA-DQw6 43-56	a
	DVG V	Y	R	A	V	T	P	Q	G	R	PDA	HLA-DQw6 43-58	a
	DSDVG V	Y	R	A	V	T	P	Q	G	R	PD	HLA-DQw6 41-57	a
	DSDVG V	Y	R	A	V	T	P	Q	G	R	PDA	HLA-DQw6 41-58	a
	DSDVG V	Y	R	A	V	T	P	Q	G	R	PDAEY	HLA-DQw6 41-60	a
	AAD	M	A	A	Q	I	T	K	R	K	WEAAH	HLA-A3 135-151	a
	TAAD	M	A	A	Q	I	T	K	R	K	WEA	HLA-A3 134-149	a
	DVGE	F	A	A	V	T	E	K	R	R	PDAEYW	HLA-DR2b 43-61	a
	T-cell epitopes	PK	Y	V	K	Q	N	T	L	K	L	AT	HA 307-319
		L	Q	A	A	P	A	L	D	K	L	HSP65 418-427	a, d
	VHF	F	K	N	I	V	T	P	R	T	P	MBP 87-99	e
	ASD	Y	K	S	A	H	K	G	F	K	GVD	MBP 131-145	a
	KG	F	K	G	V	D	A	Q	G	T	LSKI	MBP 139-153	a

References:

a: Vogt et al. 1994; b: Wucherpennig et al. 1994; c: O'Sullivan et al. 1991; d: Anderson et al. 1988; e: Martin et al. 1991

L HLA-DQA1*0501/DQB1*0301

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor residues		F,Y I,M L,V				V,L I,M Y		Y,F M,L V,I				a	
Preferred residues	A		A	A	A								
Examples for ligands	TPL	L	M	Q	<u>A</u>	L	P	M	G	A	LPQG	Invariant chain 111-126	a
	TPL	L	M	Q	<u>A</u>	L	P	M	G	A	LPQ	Invariant chain 111-125	a
	KPPKPVSKMR	M	<u>A</u>	T	<u>P</u>	L	L	M	Q	A		Invariant chain 99-117	a
	LPKPPKPVSKMR	M	<u>A</u>	T	<u>P</u>	L	L	M				Invariant chain 97-115	a
	IPE	L	N	K	V	A	R	A	A	A		Transferrin receptor 579-597	a
	DVEV	Y	R	<u>A</u>	V	T	P	L	G	P	EVAGQF	DQβ chain 43-55	a

References:

a: Falk et al. 1994 b

M HLA-DPA1*0201/DPB1*0401

		Relative position										Source	Ref.	
		1	2	3	4	5	6	7	8	9	10			
Anchor residues		F,L Y,M I,V A						F,L Y,M V,I A			V,Y I,A L		a	
Examples for ligands	EKK	Y	F	A	A	T	Q	F	E	P	L	AARL	Unknown	a
	KK	Y	F	A	A	T	Q	F	E	P	L	AARL	Unknown	a
	EKK	Y	F	A	A	T	Q	F	E	P	L		Unknown	a
	GPG	A	P	A	D	V	Q	Y	D	L	Y	LNVANRR	IL-3 Receptor α -chain 127-146	a

References:

a: Falk et al. 1994 b

Table 6 (Continued)
N HLA-DPA1*0102/DPB1*0201

												Source	Ref.
		Relative position											
		1	2	3	4	5	6	7	8	9			
Anchor residues		F,L M,V W,Y				F,L M,Y			I,A M,V			a	
Examples for ligands	ADEKKF GEP LPSQA	W L F	G S E	K Y Y	Y T I	L R L	Y F Y	E S N	I L K	A A G	RRHP RQVDG	Cattle serum albumin 152-170 Transferrin receptor 15-31 Cathepsin H 185-198	a a a

References:

a: Rötzschke and Falk 1994

Table 7 Other human class II ligands

MHC molecule	Peptide sequence	Source		Ref.
HLA-DR2 (DRB5*0101 or DRB1*1501)	NIVIKRSNSTAATNEVPEVTVFS	HLA-DQα	97-119	a
	NIVIKRSNSTAATNEV	HLA-DQα	97-112	a
	SDVGVRVAVTPQGRPDAE	HLA-DQβ	42-59	a
	DVGVRVAVTPQGRPDAE	HLA-DQβ	43-59	
	DVGVRVAVTPQGRPD	HLA-DQβ	43-57	
	RVQPKVTVYPSKTQPLQH	HLA-DRB1*1501	94-111	a
	RVQPKVTVYPSKTQ	HLA-DRB1*1501	94-108	a
	LSPIHIALNFSLDQAPVDSHGLRPALHYQ	Fibronectin receptor α	586-616	a
	DGILYQQSGGRLRRPVN	K ⁺ channel protein	173-190	a
	IQNLKEEAF LGITDEKTEG	Mannose binding protein	174-193	a
	EHHIFLGATNYIYVLNEEDLQKV	MET protooncogene	59-81	a
	QELKNKYQVPRKGIQA	Guanylate binding protein 2	434-450	a
	FPKSLHTYANILLDRRVPQTD	Apolipoprotein B100	1200-1220	a
	FPKSLHTYANILLDRRVPQ	Apolipoprotein B100	1200-1218	a
	LWDYGMSSSPHVLNR	Factor VIII	1775-1790	a
HLA-DRB1*0701	RPAGDGTFOKWASVVVPSGQ	HLA-A29	234-253	a
	RPAGDGTFOKWASVVV		234-249	a
	GDGTFOKWASVVVPSGQEQRYT		237-258	a
	GDGTFOKWASVVVPSGQE		237-254	a
	GTFQKWASVVVPSG		239-252	a
	GTFQKWASVVVPSGQ		239-253	a
	GTFQKWASVVVPSGQEQRYTCHV		239-261	a
	RETQISKNTNTQTYREN	HLA-B44	83-99	a
	RETQISKNTNTQTYREN		83-98	a
	RETQISKNTNTQTYRE		83-97	a
	RSNYTPITNPPEVTVLTNSPVELREP	HLA-DR α chain	101-126	a
	GALANIAVDKANLEIMTKRSN		58-78	a
	SLOSPITVEWRAQSESAQSKMLSGIGGFVL	HLA-DQ α chain	179-?	a
	VTQYLNATGNRWCSWSLSQAR	4F2	318-338	a
	VTQYLNATGNRWCSWSL		318-334	a
	TSILCYRKREWI	LIF receptor	854-866	a
	PAFRFTREAAQDCEV	Thromboxane-A synthase	406-420	a
	GDMYPKTSWGMVLGALCALAGVLTII	K ⁺ channel protein	492-516	a
	TPSYVAFTDTERLIGDA	Hsp 70	38-54	a
	TPSYVAFTDTERLIG		38-52	a
	VPGLYSPCRAFFNKELL	EBV MCP	1264-1282	a
	VPGLYSPCRAFFNK		1264-1277	a
	KVDLTFSKQHALLCSQADYES	Apolipoprotein B 100	1586-1608	a
	KVDLTFSKQHALLCS		1586-1600	a
	FSHDYRGSTSHRL		1942-1954	a
	LPKYFEKKRNTII		2077-2089	a
	APVLISQKLSPIYNLVPVK	Complement C9	465-483	a
	VGSDWRFLRGYHQYAYDG	HLA-A2	103-120	a
	PKPPKPVSKMRMATPLLMQALP	Invariant chain	98-119	a
	APSPLPETTENVVCALGLTV	HLA-DRα chain	182-200	a
	KHKVYACEVTHQGL	Ig kappa chain	188-201	a

Table 7 (Continued)

MHC molecule	Peptide sequence	Source		Ref.
HLA-DRB1*0801	APSPLPETTENNVVCAIG	HLA-DR α chain	182-198	a
	SETVFLPREDHLFRKFHYLPFLP	HLA-DR α chain	158-180	a
	RHNYELDEAVTLQ	HLA-DP β chain	80-92	a
	DPQSGALYISKVQKEDNSTYI	LAM Blast-1	88-108	a
	GALYISKVQKEDNSTYI		92-108	a
	DPVPKPKVIKIEKIEDMDD		129-146	a
	DPVPKPKVIKIEKIED		129-143	a
	FTFTISRLEPEDFAVYYC	Ig κ chain	63-80	a
	FTFTISRLEPEDFAV		63-77	a
	DPVEMRRLLNYQTPG	LAR	1302-1316	a
	YQLLRSMIGYIEELAPIV	LIF receptor	709-726	a
	GNHLYKWKQIPDCENVK	IFN- α receptor	271-287	a
	LPFFFLFRQAYHPNNSPVCY	IL-8 receptor	169-188	a
	RPSMLQHLLR	Ca ²⁺ release channel	2614-2623	a
	DDFMGQLLNGRVLPVNLQLGA	CD35	359-380	a
	IPRLQKIWKNYLSMNKY	CD75	106-122	a
	EPFLYILGKSRVLEAQ	Calcitonin receptor	38-53	a
	NRSEEFLLIAGKLQDGLLH	TIMP-1	101-118	a
	RSEEFLLIAGKLQDGLL		102-117	a
	SEEFLLIAGKLQDGLL		103-117	a
	NRSEEFLLIAGKL		101-112	a
	QAKFFACIKRSDGSCAWYRGAAPPKQEF	TIMP-2	187-214	a
	QAKFFACIKRSDGSCAWYR		187-205	a
	DRPFLFVVRHNPTGTVLFM	PAI-1	378-396	a
	MPHFFRLFRSTVKQVD		133-148	a
	QNFTVIFDTGSSNLWVPSVYCTSP	Cathepsin E	89-112	a
	QNFTVIFDTGSSNLWV		89-104	a
	TAFQYIIDNKGIDSDAS	Cathepsin S	189-205	a
	DEYYRLLRLVLRAREQIV	Cystatin SN	41-58	a
	EAIYDICRRNLDIERPT	Tubulin α -1 chain	207-223	a
	EAIYDICRRNLDI		207-219	a
	HELEKIKKQVEQEKCEIQAAAL	Myosin β heavy chain	1027-1047	a
	AEVYHDVAASEFF ...	α -enolase	23-?	a
	KRSFFALRDQIPDL	c-myc	371-385	a
	RQYRLKKISKEEKTPGC	K-ras	164-180	a
	KNIFHFQVNOEGLKLSNDMM	Apolipoprotein B-100	1724-1743	a
	KNIFHFQVNOEGLKLS		1724-1739	a
	YKQTVSLDIQPYSLVTTLS		1780-1799	a
	STPEFTILNTLHIPSFT		2646-2662	a
	TPEFTILNTLHIPSFTID		2647-2664	a
	TPEFTILNTLHIPSFT		2647-2662	a
	SNTKYFHKLNIPQLDF		2885-2900	a
	LPFFKFLPKYFEKKRNT		2072-2088	a
	LPFFKFLPKYFEKKR		2072-2086	a
	WNFYYSQSSPDKKL		4022-4036	a
	DVIWELLNHAQEHFGKDKSKE	Cattle transferrin	261-281	a
	DVIWELLNHAQEHFG		261-275	a
	DVIWELLNHAQEH		261-273	a
	IALLLMASQEPQRM	von Willebrand factor	617-636	a
	IALLLMASQEPQRM		617-630	a
HLA-DR11 or Dw52	SXVITLNTNVGLYXQS	Homol. Apolipoprotein	3345-3360	b
	DPXQDELQKLNAXDP	Unknown		b
	XPELNKVARAAAEVAG	Homol. Transferrin receptor	580-595	b
DR17 or DRw 52	TFDEIASGFRQGGASQ	Glucose transporter	459-474	a
	YGYTSYDTFSWAFI	Na ⁺ channel protein	384-397	a
	GQVKNNHQEDKIE	CD45	1071-1084	a
	TGHGARTSTEPTTDY	EBV gp220	592-606	a
	KELKRQYEKKLRQ	EBV tegument p140	1395-1407	a
	SPLQALDFFGNGPPVNYKTGNL	IP 30	38-59	a

References:

a: Chicz et al. 1993; b: Newcomb and Cresswell 1993

Table 8 Mouse class II motifs
A H-2E^b

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		I,L V,F Y,W			I,L V,F S		Q,N A			K,R		a, b, c	
Examples for ligands	HPPHIE	I	Q	M	L	K	N	G	K	K		β_2m 42-56	c
	DNRM	V	H	F	I	A	E	F	K	R	K	HSC70 234-248	c
	TPTL	V	E	A	A	R	N	L	G	R	VG	Serum albumin 347-361	c
	VNKE	I	Q	N	A	V	Q	G	V	K	HI	C cyt inhib. 41-55	c
	GFPT	I	Y	F	S	P	A	N	K	K	L	ER60 448-461	a
	IP	L	I	M	L	I	N	K	A	R	NKAE	Unknown	a
	YDRN	T	K	S	P	L	F	V	G	K	V	α 1-antitryp. 397-410	a
		F	A	E	F	G	T	L	K	K	AAVHYDRSG	Unknown	a
	LH	L	G	Y	L	P	N	Q	L	F	R	(human) dead box protein	a
	IPGGP	V	R	L	C	P	G	R	I	R		Cattle fetuin 342-	a
T-cell epitopes	RADL	I	A	Y	L	K	Q	A	T	K		MCC 91-103	b
	RADL	I	A	Y	L	K	Q	A	T	A	K	PCC 91-104	b
	LEDARR	L	K	A	I	Y	E	K	K	K		λ rep 12-26	e
	QD	I	L	I	R	L	F	K	S	H	PETL	SWMb 26-40	e
	VTV	L	T	A	L	G	A	I	L	K	K	SWMb 66-78	d
		L	T	A	L	G	G	I	L	K		EqMb 69-77	b
		L	T	A	L	G	T	I	L	K		MoMb 69-77	b
		I	T	A	F	N	E	G	L	K		MoHb 68-76	b
	KVFGK	C	E	L	A	A	A	M	K	R	HGLD	HEL 1-18	e
	SALLSSD	I	T	A	S	V	N	C	A	K		HEL 81-96	d
		W	V	A	W	R	N	R	C	K	GTD	HEL 108-119	d
	VEK	Y	G	P	E	A	S	A	F	T	KKMVENAK	SNase 51-70	e
	RTDKYGRG	L	A	Y	I	Y	A	D	G	K	MVN	SNase 81-100	e
	HEHQ	L	R	K	S	E	A	Q	A	K	KEKLNTW	SNase 121-140	f
		I	A	K	F	G	T	A	F	K		LLO 218-226	b

References:

a: Schild and co-workers, submitted; b: Reay et al. 1994; c: Marrack et al. 1993; d: Spouge et al. 1987; e: Altuvia et al. 1994; f: Sette et al. 1989

B H-2E^d

		Relative position									Source	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		W,Y F,I, L,V			K,R I		I,L V,G			K,R		a	
Examples for ligands	SQLELR	W	K	S	R	H	I	K	E	R		IL-2R. γ chain 168-182	a
	LELR	W	K	S	R	H	I	K	E	R		IL-2R. γ chain 170-182	a
	ERAEA	W	R	Q	K	<u>L</u>	H	G	R	L		Apo-E prec. 222-236	a
	RAEA	W	R	Q	K	<u>L</u>	H	G	R	L		Apo-E prec. 223-236	a
	AQ	F	M	W	I	<u>I</u>	R	K	R	I	QLP	Unknown	a
	SLDEH	Y	H	I	R	<u>V</u>	H	L	V	K		Similar Apolipoprotein B 2211-2224	a
	GQFY	F	L	I	R	K	R	I	H	L	R	C. elegans cDNA homol. 74-87	a
	LV	V	D	N	G	S	G	M	C	K	AGF	Actin B 8-21	a
T-cell epitopes	ALWFRNH	F	V	F	G	G	G	T	K	V	TV	Ig lambda 91-108	b
	KYLEFISEA	I	I	H	V	L	H	S	R			SWM 102-118	c
	NKALE	L	F	R	K	D	I	A	A	K	Y	SWM 132-146	d
	W	V	A	W	R	N	R	C	K	G	TD	HEL 108-119	c
	A	Y	V	Y	K	P	N	N	T	H	EQHLRKSE	SNase 112-129	e
	SS	F	E	R	F	E	I	F	P	K		FLU PR/8 HA 109-119	c
	LEDARR	L	K	A	I	Y	E	K	K	K		λ rep 12-26	c
	EK	I	R	L	R	P	G	G	K	K	K	HIV-1 gag p17 17-28	f

References:

a: Schild and co-workers, submitted; b: Bogen et al. 1986; c: Spouge et al. 1987; d: O'Sullivan et al. 1991; e: Chiczy et al. 1992; f: Sette et al. 1989

Table 8 (Continued)
C H-2E^a

		Relative position									Comments	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		I,V L			L,I V		Q,N			K,R	This motif has been predicted based on prediction of pocket structure and comparison with H-2E ^k and H-2E ^d motifs	a	
		Source											
Examples for ligands		L	Y	V	L	K	I	G	K	K	DG	Carboxypeptidase A 44–54	b
	HPPHIE	I	Q	M	L	K	N	G	K	K		β ₂ 42–56	b
	EGEC	V	E	W	L	H	R	Y	L	K	NG	H-2L ^d 160–174	b
	MQKEITA	L	A	P	S	T	M	K	I	K	II	β-actin 286–303	b
	CT	F	A	I	C	W	L	P	F	H	VFFL	Substance P receptor 255–269	b
	EGSLI	V	E	K	I	M	Q	S	S	S	E	HSP60 478–492	b
T-cell epitope		DL	I	A	Y	L	K	Q	A	T	K	MCC 93–103	c, d

References:

a: Schild and co-workers, submitted; b: Marrack et al. 1993; c: Altuvia et al. 1994; d: Reay et al. 1994

D H-2E^b

		Relative position									Comments	Ref.	
		1	2	3	4	5	6	7	8	9			
Anchor or preferred residues		W,F Y			L,I F,V		Q,N, A			K,R		This motif has been predicted based on prediction of pocket structure and comparison with H-2E ^a and H-2E ^b motifs	a
		Source											
Examples for ligands	SPSYV	Y	H	Q	F	E	R	R	A	K	YK	MuLV env protein 454-469	b
	SPSYV	Y	H	Q	F	E	R	R	A	K	YKREPVSL	MuLV env protein 454-475	b
	SPSYV	Y	H	Q	F	E	R	R	A	K		MuLV env protein 454-467	b
	GK	Y	L	Y	E	I	A	R	R	H	PYFY	BSA 141-155	b
	XPQS	Y	L	I	H	E	X	X	X	I	S	Unknown	b
T-cell epitopes	RTDKYGRG	L	A	Y	I	Y	A	D	G	K	MVN	SNase 81-100	c, d
	DL	I	A	Y	L	K	Q	A	T	K		MCC 93-103	c, d

References:

a: Schild and co-workers, submitted; b: Rudensky et al. 1991; c: Altuvia et al. 1994; d: Reay et al. 1994

Table 9 Other mouse class II ligands

MHC Molecule	Peptide sequence	Source		Ref.
H-2A ^b	HNEGIFYVCPGPHRP	MuLV env	145-158	a
	ASFEAQGALANIAVDKA	H-2E α	52-68	a
	KPVSQMRMATPLLMR	Invariant chain	86-100	a
	NYNAYNATPATLAVD	Unknown		a, b
	RPDAEYWNSQPE	H-2A β	55-66	b
	XNADFCKTPATLTVDKP	IgG V μ	59-74	b
H-2A ^s	IRLKITDSGPRVPIGPN	MuLV env	255-269	b
	IRLKITDSGPRVPIG	MuLV env	255-267	b
	WQSQSITCNVAHPASST	IgG2a	194-210	b
	NVEVHTAQQTQTHREDY	IgG2a	281-296	b
	KPTEVSGKLVHANFGT	Transferrin receptor	203-218	b
	XPYMFADKVVHLPGSQ	Unknown		b
H-2A ^d	WANLMEKIQASVATNPI	Apo-E	268-284	c
	WANLMEKIQASVATNP	Apo-E	268-283	c
	DAYHSRAIQVVRARKQ	Cys-C	40-55	c
	ASFEAQGALANIAVDKA	H-2I-E α ^d	52-68	c
	ASFEAQGALANIAVDK	H-2I-E α ^{cd}	52-67	c
	EEQTOQIRLQAEIFQAR	Apo-E	236-252	c
	EQTQQIRLQAEIFQAR	Apo-E	237-252	c
	KPVSQMRMATPLLMRPM	Li	85-101	c
	VPQLNQMVRTAAEVAGQX	Tf recp.	442-459	c
	ISQAVHAAHAEINE	Ovalbumin	323-336	c
	LEDARRLKAIYEKKK	λ repressor	12-26	c
H-2A ^k	DGSTDYGILQINSR	Hen egg lysozyme	48-61	d
	DGSTDYGILQINS		48-60	d
	DGSTDYGILQINSRW		48-62	d
	DYGILQINSRWW (C)		52-63 (64)	d
	IIANDQGNRTTPSY	hsp70	28-41	d
	TPRRGEVYTCHVEHP	H-2I-A ^k β chain	165-179	d
	KVHGSLARAGKVRGQTPKVAQK	S30 ribosomal protein	75-96	d
	AGKVRGQTPKVAQKQEKKKKT		83-103	d
	EPLVPLDNHIPPENAQPG	Ryudocan	84-100	d
	XQLGAQNEMLXPL	Unknown		e
	XXXKGTDFQLNQL	Transferrin	100-113	e
	KGTDQFQLNQLGKKK	Transferrin	103-117	e
	YVRFDSFVGEYRAVT	H-2A β ^k	37-51	e
	XPLALQFAELPVNKG	Unknown		e
	XNLRFDSDVGEFRAV	H-2E β ^k	33-47	e
	EDENLYEGLNLDXSMYE	MBI	177-194	e
	XXLYNKGIMGEDSYPY	Cathepsin H	77-92	e
	SYLDAXVXEQLAT	Fc ϵ -Receptor II	298-310	e
H-2A ^{g7}	XXXHFVHQFQPFcyF	H-2A β ^k	3-17	e
	QFQPFXYFTNT	H-2A β ^k	10-20	e
	KPKATAEQLKTVMDD	Serum albumin	560-574	f
	GHNVVTAIRNQOEG	Transferrin	55-68	f
	ETTEESLRNYYEQ	hnRNP B1 & A2	31-43	f
	VVMRDPASKRSRGFGF	hnRNP A2 & B1	51-66	f
	VVMRDPQTKRSRGFGF	hnRNP A1	44-59	f
	PKEPEQLRKLFIGGL	hnRNP A1	7-21	f
	VVYPWTQRYFDSF	β Globin major	33-45	f

References:

a: Rudensky et al. 1991; b: Rudensky et al. 1992; c: Hunt et al. 1992b; d: Nelson et al. 1992; e: Marrack et al. 1993; f: Reich et al. 1994

References

- Achour, A., Picard, O., Zagury, D., Sarin, P. S., Gallo, R. C., Nagler, P. H., and Goldstein, A. L. HGP-30, a synthetic analog of human immunodeficiency virus (HIV) (p17), is a target for cytotoxic T lymphocytes in HIV-infected individuals. *Proc Natl Acad Sci USA* 87: 7045–7049, 1990
- Alsheikhly, A. R. Interaction of in vitro- and in vivo-generated cytotoxic T Cells with SV40 T antigen – analysis with synthetic peptides. *Scand J Immunol* 39: 467–479, 1994
- Altuvia, Y., Berzofsky, J. A., Rosenfeld, R., and Margalit, H. Sequence features that correlate with MHC restriction. *Mol Immunol* 31: 1–19, 1994
- Anderson, D. C., van Schoten, W. C. A., Barry, M. E., Janson, A. A. M., Buchanan, T. M., and De Vries, R. R. P. A Mycobacterium leprae-specific human T cell epitope cross-reactive with an HLA-DR2 peptide. *Science* 242: 259, 1988
- Banks, T. A., Nair, S., and Rouse, B. T. Recognition by and in vitro induction of cytotoxic T-lymphocytes against predicted epitopes of the immediate-early protein-ICP27 of Herpes-Simplex virus. *J Virol* 67: 613–616, 1993
- Bastin, J., Rothbard, J., Davey, J., Jones, I., and Townsend, A. Use of synthetic peptides of influenza nucleoprotein to define epitopes recognized by class I-restricted cytotoxic T lymphocytes. *J Exp Med* 165: 1508–1523, 1987
- Beauverger, P., Buckland, R., and Wild, T. F. Measles-virus antigens induce both type-specific and canine-distemper virus cross-reactive cytotoxic T-lymphocytes in mice: localization of a common L₄-restricted nucleoprotein epitope. *J Gen Virol* 74: 2357–2363, 1993
- Beauverger, P., Buckland, R., and Wild, T. F. Measles hemagglutinin induces an L₄-restricted CD8⁺ cytotoxic T lymphocyte response to two specific epitopes. *Virology* 200: 281–283, 1994
- Bednarek, M. A., Sauma, S. Y., Gammon, M. C., Porter, G., Tamhanakar, S., Williamson, A. R., and Zweerink, H. J. The minimum peptide epitope from the influenza matrix protein. Extra and intracellular loading of HLA-A2. *J Immunol* 147: 4047–4053, 1991
- Bergmann, C., McMillan, M., and Stohman, S. Characterization of the L₄-restricted cytotoxic T-lymphocyte epitope in the mouse hepatitis-virus nucleocapsid protein. *J Virol* 67: 7041–7049, 1993a
- Bergmann, C., Stohmann, S. A., and McMillan, M. An endogenously synthesized decamer peptide efficiently primes cytotoxic T-cells specific for the HIV-1 envelope glycoprotein. *Eur J Immunol* 23: 2777–2781, 1993b
- Bentoletti, A., Chisari, F. V., Penna, A., Guilhot, S., Galati, L., Missale, G., Fowler, P., Schlicht, H. J., Vitiello, A., Chesnut, R. C., Fiaccadori, F., and Ferrari, C. Definition of a minimal optimal cytotoxic T-cell epitope within the hepatitis-B virus nucleocapsid protein. *J Virol* 67: 2376–2380, 1993
- Bentoletti, A., Costanzo, A., Chisari, F. V., Levrero, M., Artini, M., Seue, A., Penna, A., Giuberti, T., Fiaccadori, F., and Ferrari, C. Cytotoxic T lymphocyte response to a wild type hepatitis B virus epitope in patients chronically infected by variant viruses carrying substitutions within the epitope. *J Exp Med* 180: 933–943, 1994
- Blum-Tirouvanziam, U., Beghdadi-Rais, C., Roggero, M. A., Valmori, D., Berholet, S., Bron, C., Fasel, N., and Corradin, G. Elicitation of specific cytotoxic T cells by immunization with malaria soluble synthetic polypeptides. *J Immunol* 153: 4134–4141, 1994
- Bodmer, J. G., Marsh, S. G. E., Albert, E. D., Bodmer, W. F., Dupont, B., Erlich, H. A., Mach, B., Mayr, W. R., Parham, P., Sasazuki, T., Schreuder, G. M. T., Strominger, J. L., Svejgaard, A., and Terasaki, P. I. Nomenclature for factors of the HLA system, 1994. *Tissue Antigens* 44: 1–18, 1994
- Bogen, B., Snodgrass, R., Briand, J. P., and Hannestad, K. Synthetic peptides and beta-chain gene rearrangements reveal a diversified T cell repertoire for a lambda light chain third hypervariable region. *Eur J Immunol* 16: 1379–1384, 1986
- Bonneau, R. H., Salvucci, L. A., Johnson, D. C., and Tevethia, S. S. Epitope specificity of H-2Kb-restricted, HSV-1-cross-reactive, and HSV-2-cross-reactive cytotoxic T-lymphocyte clones. *Virology* 195: 62–70, 1993
- Braciale, T. J., Braciale, V. L., Winkler, M., Stroynowski, I., Hood, L., Sambrook, J., and Gething, M.-J. On the role of the transmembrane anchor sequence of influenza hemagglutinin in target cell recognition by class I MHC-restricted, hemagglutinin-specific cytolytic T lymphocytes. *J Exp Med* 166: 678–692, 1987
- Brichard, V., Van Pel, A., Wölfel, T., Wölfel, C., De Plaen, E., Lethe, B., Coulie, P., and Boon, T. The tyrosinase gene codes for an antigen recognized by autologous cytolytic T-lymphocytes on HLA-A2 melanomas. *J Exp Med* 178: 489–495, 1993
- Brooks, J. M., Murray, R. J., Thomas, W. A., Kurilla, M. G., and Rickinson, A. B. Different HLA-B27 subtypes present the same immunodominant Epstein-Barr virus peptide. *J Exp Med* 178: 879–887, 1993
- Brown, E. L., Wooters, J. L., Ferenz, C. R., O'Brien, C. M., Hewick, R. M., and Herrmann, S. H. Characterization of peptide binding to the murine MHC class I H-2K^b molecule – sequencing of the bound peptides and direct binding of synthetic peptides to isolated class I molecules. *J Immunol* 153: 3079–3092, 1994
- Brown, J. H., Jardetzky, T. S., Gorga, J. C., Stern, L. J., Urban, R. G., Strominger, J. L., and Wiley, D. C. Three-dimensional structure of the human class II histocompatibility antigen HLA-DR1. *Nature* 364: 33–39, 1993
- Burrows, S. R., Sculley, T. B., Misko, I. S., Schmidt, C., and Moss, D. J. An Epstein-Barr virus-specific cytotoxic T cell epitope in EBV nuclear antigen 3 (EBNA 3). *J Exp Med* 171: 345–349, 1990
- Buseyne, F., McChesney, M., Porrot, F., Kovarik, S., Guy, B., and Riviere, Y. Gag-specific cytotoxic T-lymphocytes from human immunodeficiency-virus type-1-infected individuals: Gag epitopes are clustered in three regions of the p24gag protein. *J Virol* 67: 694–702, 1993
- Buseyne, F. and Riviere, Y. HIV-specific CD8⁺ T-cell immune responses and viral replication. *Aids* 7: S81–S85, 1993
- Buus, S., Sette, A., Colon, S. M., Miles, C., and Grey, H. M. The relation between major histocompatibility complex (MHC) restriction and the capacity of Ia to bind immunogenic peptides. *Science* 235: 1353–1358, 1987
- Cao, W. X., Myers-Powell, B. A., and Braciale, T. J. Recognition of an immunoglobulin Vh epitope by influenza virus-specific class I major histocompatibility complex-restricted cytolytic T lymphocytes. *J Exp Med* 179: 195–202, 1994
- Carbone, F. R., Moore, M. W., Sheil, J. M., and Bevan, M. J. Induction of cytotoxic T lymphocytes by primary in vitro stimulation with peptides. *J Exp Med* 167: 1767–1779, 1988
- Celis, E., Tsai, V., Crimi, C., DeMars, R., Wentworth, P. A., Chesnut, R. W., Grey, H. M., Sette, A., and Serra, H. M. Induction of antitumor cytotoxic T-lymphocytes in normal humans using primary cultures and synthetic peptide epitopes. *Proc Natl Acad Sci USA* 91: 2105–2109, 1994
- Cerrone, M. C., Ma, J. J., and Stephens, R. S. Cloning and sequence of the gene for heat-shock protein-60 from Chlamydia trachomatis and immunological reactivity of the protein. *Infect Immun* 59: 79–90, 1991
- Cerundolo, V., Elliott, T., Elvin, J., Bastin, J., Rammensee, H.-G., and Townsend, A. The binding affinity and dissociation rates of peptides for class I major histocompatibility complex molecules. *Eur J Immunol* 21: 2069–2075, 1991
- Chicz, R. M., Urban, R. G., Lane, W. S., Gorga, J. C., Stern, L. J., Vignali, D. A. A., and Strominger, J. L. Predominant naturally processed peptides bound to HLA-DR1 are derived from MHC-related molecules and are heterogeneous in size. *Nature* 358: 764–768, 1992
- Chicz, R. M., Urban, R. G., Gorga, J. C., Vignali, D. A. A., Lane, W. S., and Strominger, J. L. Specificity and promiscuity among naturally processed peptides bound to HLA-DR alleles. *J Exp Med* 178: 27–47, 1993
- Corr, M., Boyd, L. F., Frankel, S. R., Kozlowski, S., Padlan, E. A., and Margulies, D. H. Endogenous peptides of a soluble major histocompatibility complex class-I molecule, H-2L^ds-sequence motif, quantitative binding, and molecular modeling of the complex. *J Exp Med* 176: 1681–1692, 1992

- Corr, M., Boyd, L. F., Padlan, E. A., and Margulies, D. H. H-2D^d exploits a 4 residue peptide binding motif. *J Exp Med* 178: 1877-1892, 1993
- Cossins, J., Gould, K. G., Smith, M., Driscoll, P., and Brownlee, G. G. Precise prediction of a K^b-restricted cytotoxic T-cell epitope in the NS1 protein of influenza-virus using an MHC allele-specific motif. *Virology* 193: 289-295, 1993
- Coulie, P. G., Brichard, V., Van Pel, A., Wölfel, T., Schneider, J., Traversari, C., Mattei, S., De Plaen, E., Lurquin, C., Szikora, J. P., Renauld, J. C., and Boon, T. A new gene coding for a differentiation antigen recognized by autologous cytolytic T-lymphocytes on HLA-A2 melanomas. *J Exp Med* 180: 35-42, 1994
- Cox, A. L., Skipper, J., Chen, Y., Henderson, R. A., Darrow, T. L., Shabanowitz, J., Engelhard, V. H., Hunt, D. F., and Slingluff, C. L. Identification of a peptide recognized by five melanoma-specific human cytotoxic T cell lines. *Science* 264: 716-719, 1994
- Cresswell, P. Assembly, transport, and function of MHC class II molecules. *Annu Rev Immunol* 12: 259-293, 1994
- Culmann, B., Gomard, E., Kieny, M. P., Guy, B., Dreyfus, F., Saimot, A. G., Sereni, D., Sicard, D., and Levy, J. P. 6 epitopes reacting with human cytotoxic CD8⁺ T-cells in the central region of the HIV-1 nef protein. *J Immunol* 146: 1560-1565, 1991
- Dai, L. C., West, K., Littau, R., Takahashi, K., and Ennis, F. A. Mutation of human immunodeficiency virus type 1 at amino acid 585 on gp41 results in loss of killing by CD8⁺ A24-restricted cytotoxic T lymphocytes. *J Virol* 66: 3151-3154, 1992
- De Bergeyck, V., De Plaen, E., Chomez, P., Boon, T., and Van Pel, A. An intracisternal A-particle sequence codes for an antigen recognized by syngeneic cytolytic T lymphocytes on a mouse spontaneous leukemia. *Eur J Immunol* 24: 2203-2212, 1994
- Deckhut, A. M., Lippolis, J. D., and Tevethia, S. S. Comparative analysis of core amino-acid-residues of H-2D^b-restricted cytotoxic T-lymphocyte recognition epitopes in Simian virus 40 T antigen. *J Virol* 66: 440-447, 1992
- DiBrino, M., Parker, K. C., Shiloach, J., Knierman, M., Lukszo, J., Turner, R. V., Biddison, W. E., and Coligan, J. E. Endogenous peptides bound to HLA-A3 possess a specific combination of anchor residues that permit identification of potential antigenic peptides. *Proc Natl Acad Sci USA* 90: 1508-1512, 1993a
- DiBrino, M., Tsuchida, T., Turner, R. V., Parker, K. C., Coligan, J. E., and Biddison, W. E. HLA-A1 and HLA-A3 T-cell epitopes derived from influenza virus proteins predicted from peptide binding motifs. *J Immunol* 151: 5930-5935, 1993b
- DiBrino, M., Parker, K. C., Shiloach, J., Turner, R. V., Tsuchida, T., Garfield, M., Biddison, W. E., and Coligan, J. E. Endogenous peptides with distinct amino acid anchor residue motifs bind to HLA-A1 and HLA-B8. *J Immunol* 152: 620-631, 1994
- Dick, L. R., Aldrich, C., Jameson, S. C., Moomaw, C. R., Pramanik, B. C., Doyle, C. K., Demartino, G. N., Bevan, M. J., Forman, J. M., and Slaughter, C. A. Proteolytic processing of ovalbumin and beta-galactosidase by the proteasome to yield antigenic peptides. *J Immunol* 152: 3884-3894, 1994
- Eberl, G., Sabbatini, A., Servis, C., Romero, P., Maryanski, J. L., and Corradin, G. MHC class I H-2K^d-restricted antigenic peptides: additional constraints for the binding motif. *Int Immunol* 5: 1489-1492, 1993
- Engelhard, V. H., Appella, E., Benjamin, D. C., Bodnar, W. M., Cox, A. L., Chen, Y., Henderson, R. A., Huczko, E. L., Michel, H., Sakaguchi, K., Shabanowitz, J., Sevilir, N., Slingluff, C. L., and Hunt, D. F. Mass spectrometric analysis of peptides associated with the human class-I MHC molecules HLA-A2.1 and HLA-B7 and identification of structural features that determine binding. In A. Sette (ed.): *Naturally Processed Peptides*, Karger, pp. 39-62, 1993
- Engelhard, V. H. Structure of peptides associated with MHC class I molecules. *Curr Opin Immunol* 6: 13-23, 1994
- Falk, K., Rötzschke, O., and Rammensee, H.-G. Cellular peptide composition governed by major histocompatibility complex class I molecules. *Nature* 348: 248-251, 1990
- Falk, K., Rötzschke, O., Deres, K., Metzger, J., Jung, G., and Rammensee, H.-G. Identification of naturally processed viral non-peptides allows their quantification in infected cells and suggests an allele-specific T cell epitope forecast. *J Exp Med* 174: 425-434, 1991a
- Falk, K., Rötzschke, O., Stevanović, S., Jung, G., and Rammensee, H.-G. Allele-specific motifs revealed by sequencing of self-peptides eluted from MHC molecules. *Nature* 351: 290-296, 1991b
- Falk, K., Rötzschke, O., Grahovac, B., Schendel, D., Stevanović, S., Gnau, V., Jung, G., Strominger, J. L., and Rammensee, H.-G. Allele-specific peptide ligand motifs of HLA-C molecules. *Proc Natl Acad Sci USA* 90: 12005-12009, 1993a
- Falk, K., Rötzschke, O., Grahovac, B., Schendel, D., Stevanović, S., Jung, G., and Rammensee, H.-G. Peptide motifs of HLA-B35 and HLA-B37 molecules. *Immunogenetics* 38: 161-162, 1993b
- Falk, K., Rötzschke, O., Stevanović, S., Gnau, V., Sparbier, K., Jung, G., Rammensee, H.-G., and Walden, P. Analysis of a naturally occurring HLA class I-restricted viral epitope. *Immunology* 82: 337-342, 1994a
- Falk, K., Rötzschke, O., Stevanović, S., Jung, G., and Rammensee, H.-G. Pool sequencing of natural HLA-DR, DQ, and DP ligands reveals detailed peptide motifs, constraints of processing, and general rules. *Immunogenetics* 39: 230-242, 1994b
- Falk, K., Rötzschke, O., Takiguchi, M., Grahovac, B., Gnau, V., Stevanović, S., Jung, G., and Rammensee, H.-G. Peptide motifs of HLA-A1, -A11, -A31, and -A33 molecules. *Immunogenetics* 40: 238-241, 1994c
- Falk, K., Rötzschke, O., Takiguchi, M., Gnau, V., Stevanović, S., Jung, G., and Rammensee, H.-G. Peptide motifs of HLA-B51, -B52, and -B78 molecules and implications for Behçet's disease. *Int Immunol* 7: 223-228, 1995a
- Falk, K., Rötzschke, O., Takiguchi, M., Gnau, V., Stevanović, S., Jung, G., and Rammensee, H.-G. Peptide motifs of HLA-B38 and B39 molecules. *Immunogenetics* 41: 162-164, 1995b
- Falk, K., Rötzschke, O., Takiguchi, M., Gnau, V., Stevanović, S., Jung, G., and Rammensee, H.-G. Peptide motifs of HLA-B58, B60, B61, and B62 molecules. *Immunogenetics* 41: 165-168, 1995c
- Falk, K. and Rötzschke, O. Consensus motifs and peptide ligands of MHC class I molecules. *Sem Immunol* 5: 81-94, 1993
- Feltkamp, M. C. W., Smits, H. L., Vierboom, M. P. M., Minnaar, R. P., Dejongh, B. M., Drijfhout, J. W., Tersmette, J., Melief, C. J. M., and Kast, W. M. Vaccination with cytotoxic T-lymphocyte epitope-containing peptide protects against a tumor induced by human papillomavirus type-16-transformed cells. *Eur J Immunol* 23: 2242-2249, 1993
- Fischer Lindahl, K. F., Hermel, E., Loveland, B. E., and Wang, C. R. Maternally transmitted antigen of mice - a model transplantation antigen. *Annu Rev Immunol* 9: 351-372, 1991
- Fleischhauer, K., Wallny, H.-J., Avila, D., Vilbois, F., Traversari, C., and Bordignon, C. Characterization of natural peptide ligands for HLA-B44. *Tissue Antigens*, in press
- Franco, M. A., Prieto, I., Labbe, M., Poncet, D., Borrás-Cuesta, F., and Cohen, J. An immunodominant cytotoxic T cell epitope on the VP7 rotavirus protein overlaps the H2 signal peptide. *J Gen Virol* 74: 2579-2586, 1993
- Franco, M. A., Lefevre, P., Willems, P., Lintermanns, P., Tosser, G., and Cohen, J. Identification of cytotoxic T cell epitopes on the Vp3 and Vp6 rotavirus proteins. *J Gen Virol* 75: 589-596, 1994
- Fremont, D. H., Matsamura, M., Siura, E. A., Peterson, P. A., and Wilson, I. A. Crystal structures of two viral peptides in complex with murine MHC class I H-2K^b. *Science* 257: 919-927, 1992
- Frumonto, G., Harris, P. E., Gawinowicz, M. A., Suciu-Foca, N., and Pernis, B. Sequence of a prominent 16-residue self-peptide bound to HLA-B27 in a lymphoblastoid cell line. *Cell Immunol* 152: 623-626, 1993
- Gaugler, B., Van den Eynde, B., Van der Bruggen, P., Romero, P., Gaforio, J. J., De Plaen, E., Leibe, B., Brasseur, F., and Boon, T. Human gene MAGE-3 codes for an antigen recognized on a melanoma by autologous cytolytic T-lymphocytes. *J Exp Med* 179: 921-930, 1994
- Gavin, M. A., Gilbert, M. J., Riddell, S. R., Greenberg, P. D., and Bevan, M. J. Alkali hydrolysis of recombinant proteins allows for the rapid identification of class-I MHC-restricted CTL epitopes. *J Immunol* 151: 3971-3980, 1993

- Gavioli, R., Kurilla, M. G., De Campos-Lima, P. O., Wallace, L. E., Dolcetti, R., Murray, R. J., Rickinson, A. B., and Masucci, M. G. Multiple HLA A11-restricted cytotoxic T-lymphocyte epitopes of different immunogenicities in the Epstein-Barr virus-encoded nuclear antigen 4. *J Virol* 67: 1572–1578, 1993
- Geluk, A., Van Meijgaarden, K. E., Janson, A. A. M., Drijfhout, J. W., Melen, R. H., De Vries, R. R. P., and Ottenhoff, T. H. M. Functional analysis of DR17(DR3)-restricted mycobacterial T-cell epitopes reveals DR17-binding motif and enables the design of allele-specific competitor peptides. *J Immunol* 149: 2864–2871, 1992
- Geluk, A., Van Meijgaarden, K. E., Southwood, S., Oseroff, C., Drijfhout, J. W., De Vries, R. R. P., Ottenhoff, T. H. M., and Sette, A. HLA-DR3 molecules can bind peptides carrying two alternative specific submotifs. *J Immunol* 152: 5742–5748, 1994
- Goeh, F., McMichael, A., and Rothbard, J. Recognition of influenza A matrix protein by HLA-A2-restricted cytotoxic T lymphocytes. Use of analogues to orientate the matrix peptide in the HLA-A2 binding site. *J Exp Med* 168: 2045–2057, 1988
- Gould, K., Cossins, J., Bastin, J., Brownlee, G. G., and Townsend, A. A 15 amino acid fragment of influenza nucleoprotein synthesized in the cytoplasm is presented to class I-restricted cytotoxic T lymphocytes. *J Exp Med* 170: 1051–1056, 1989
- Gould, K. G., Scofield, H., Townsend, A. R., Bastin, J., and Brownlee, G. G. Mouse H-2k-restricted cytotoxic T cells recognize antigenic determinants in both the HA1 and HA2 subunits of the influenza A/PR/8/34 hemagglutinin. *J Exp Med* 166: 693–701, 1987
- Gould, K. G., Scofield, H., and Brownlee, G. G. Characterization of two distinct major histocompatibility complex class I K^k-restricted T-cell epitopes within the Influenza A/PR/8/34 virus hemagglutinin. *J Virol* 65: 5401–5409, 1991
- Gregersen, P. K., Silver, J., and Winchester, R. J. The shared epitope hypothesis. An approach to understanding the molecular genetics of susceptibility to rheumatoid arthritis. *Arthritis Rheum* 30: 1205–1213, 1987
- Guo, H. C., Jardetzky, T. S., Garrett, T. P. J., Lane, W. S., Strominger, J. L., and Wiley, D. C. Different length peptides bind to HLA-Aw68 similarly at their ends but bulge out in the middle. *Nature* 360: 364–366, 1992
- Guo, H. C., Madden, D. R., Silver, M. L., Jardetzky, T. S., Gorga, J. C., Strominger, J. L., and Wiley, D. C. Comparison of the P2 specificity pocket in three human histocompatibility antigens – HLA-A*6801, HLA-A*0201, and HLA-B*2705. *Proc Natl Acad Sci USA* 90: 8053–8057, 1993
- Hammer, J., Takacs, B., and Sinigaglia, F. Identification of a motif for HLA-DR1 binding peptides using M13 display libraries. *J Exp Med* 176: 1007–1013, 1992
- Hammer, J., Valsasini, P., Tolba, K., Bolin, D., Higelin, J., Takacs, B., and Sinigaglia, F. Promiscuous and allele-specific anchors in HLA-DR-binding peptides. *Cell* 74: 197–203, 1993
- Hammer, J., Bono, E., Gallazzi, F., Belunis, C., Nagy, Z., and Sinigaglia, F. Precise prediction of MHC class II-peptide interaction based on peptide side chain scanning. *J Exp Med* 180: 2353–2358, 1994
- Harpur, A. G., Ziemiecki, A., Wilks, A. F., Falk, K., Röttschke, O., and Rammensee, H.-G. A prominent natural H-2K^d ligand is derived from protein-tyrosine kinase JAK1. *Immunol Lett* 35: 235–238, 1993
- Harris, P. E., Colovai, A., Liu, Z., Favara, R. D., and Suciu-Foca, N. Naturally processed HLA class I bound peptides from c-myc-transfected cells reveal allele-specific motifs. *J Immunol* 151: 5966–5974, 1993
- Henderson, R. A., Michel, H., Sakaguchi, K., Shabanowitz, J., Appella, E., Hunt, D. F., and Engelhard, V. H. HLA-A2.1-associated peptides from a mutant cell line – a 2nd pathway of antigen presentation. *Science* 255: 1264–1266, 1992
- Henderson, R. A., Cox, A. L., Sakaguchi, K., Appella, E., Shabanowitz, J., Hunt, D. F., and Engelhard, V. H. Direct identification of an endogenous peptide recognized by multiple HLA-A2.1-specific cytotoxic T cells. *Proc Natl Acad Sci USA* 90: 10275–10279, 1993
- Hill, A. V. S., Elvin, J., Willis, A. C., Aidoo, M., Allsopp, C. E. M., Goeh, F. M., Gao, X. M., Takiguchi, M., Greenwood, B. M., Townsend, A. R. M., McMichael, A. J., and Whittle, H. C. Molecular analysis of the association of HLA-B53 and resistance to severe malaria. *Nature* 360: 434–439, 1992
- Hill, C. M., Liu, A., Marshall, K. W., Mayer, J., Jorgensen, B., Yuan, B., Cubbon, R. M., Nichols, E. A., Wicker, L. S., and Rothbard, J. B. Exploration of requirements for peptide binding to HLA DRB1*0101 and DRB1*0401. *J Immunol* 152: 2890–2898, 1994
- Hosmalin, A., Clerici, M., Houghton, R., Pendleton, C. D., Felxner, C., Lucey, D. R., Moss, B., Germain, R. N., Shearer, G. M., and Berzofsky, J. A. An epitope in human immunodeficiency virus 1 reverse transcriptase recognized by both mouse and human cytotoxic T lymphocytes. *Proc Natl Acad Sci USA* 87: 2344–2348, 1990
- Howard, J. C. and Seelig, A. Antigen-processing – peptides and the proteasome. *Nature* 365: 211–212, 1993
- Huczko, E. L., Bodnar, W. M., Benjamin, D., Sakaguchi, K., Zhu, N. Z., Shabanowitz, J., Henderson, R. A., Appella, E., Hunt, D. F., and Engelhard, V. H. Characteristics of endogenous peptides eluted from the class-I MHC molecule HLA-B7 determined by mass spectrometry and computer modeling. *J Immunol* 151: 2572–2587, 1993
- Huet, S., Nixon, D. F., Rothbard, J. B., Townsend, A., Ellis, S. A., and McMichael, A. J. Structural homologies between two HLA B27-restricted peptides suggest residues important for interaction with HLA B27. *Int Immunol* 2: 311–316, 1990
- Hunt, D. F., Henderson, R. A., Shabanowitz, J., Sakaguchi, K., Michel, H., Sevilir, N., Cox, A. L., Appella, E., and Engelhard, V. H. Characterization of peptides bound to the class I MHC molecule HLA-A2.1 by mass spectrometry. *Science* 255: 1261–1263, 1992a
- Hunt, D. F., Michel, H., Dickinson, T. A., Shabanowitz, J., Cox, A. L., Sakaguchi, K., Appella, E., Grey, H. M., and Sette, A. Peptides presented to the immune system by the murine class II major histocompatibility complex molecule I-A^d. *Science* 256: 1817–1820, 1992b
- Jackson, M. R., Cohendoy, M. F., Peterson, P. A., and Williams, D. B. Regulation of MHC class-I transport by the molecular chaperone, calnexin (P88, IP90). *Science* 263: 384–387, 1994
- Jackson, M. R. and Peterson, P. A. Assembly and intracellular transport of MHC class-I molecules. *Annu Rev Cell Biol* 9: 207–235, 1993
- Jardetzky, T. S., Lane, W. S., Robinson, R. A., Madden, D. R., and Wiley, D. C. Identification of self peptides bound to purified HLA-B27. *Nature* 353: 326–329, 1991
- Johnson, R. P., Trocha, A., Buchanan, T. M., and Walker, B. D. Recognition of a highly conserved region of human immunodeficiency virus type 1 gp 120 by an HLA-Cw4-restricted cytotoxic T-lymphocyte clone. *J Virol* 67: 438–445, 1993
- Joyce, S., Tabaczewski, P., Angeletti, R. H., Nathanson, S. G., and Stroyanowski, I. A nonpolymorphic major histocompatibility complex class Ib molecule binds a large array of diverse self-peptides. *J Exp Med* 179: 579–588, 1994
- Kast, W. M., Offringa, R., Peters, P. J., Voordouw, A. C., Melen, R. H., Van der Eb, A. J., and Melief, C. J. M. Eradication of adenovirus E1-induced tumors by E1A-specific cytotoxic T lymphocytes. *Cell* 59: 603–614, 1989
- Kast, W. M., Roux, L., Curren, L., Blom, H. J. J., Voordouw, A. C., Melen, R. H., Kolakofsky, D., and Melief, C. J. M. Protection against lethal Sendai virus infection by in vivo priming of virus-specific cytotoxic T lymphocytes with a free synthetic peptide. *Proc Natl Acad Sci USA* 88: 2283–2287, 1991
- Kast, W. M., Brandt, R. M. P., Sidney, J., Drijfhout, J. W., Kubo, R. T., Grey, H. M., Melief, C. J. M., and Sette, A. Role of HLA-A motifs in identification of potential CTL epitopes in human papillomavirus type 16 E6 and E7 proteins. *J Immunol* 152: 3904–3912, 1994
- Kawakami, Y., Eliyahu, S., Delgado, C. H., Robbins, P. F., Rivoltini, L., Topalian, S. L., Miki, T., and Rosenberg, S. A. Cloning of the gene coding for a shared human-melanoma antigen recognized by autologous T-cells infiltrating into tumor. *Proc Natl Acad Sci USA* 91: 3515–3519, 1994a
- Kawakami, Y., Eliyahu, S., Delgado, C. H., Robbins, P. F., Sakaguchi, K., Appella, E., Yannelli, J. R., Adema, G. J., Miki, T., and Rosenberg, S. A. Identification of a human-melanoma antigen

- recognized by tumor-infiltrating lymphocytes associated with in vivo tumor rejection. *Proc Natl Acad Sci USA* 91: 6458-6462, 1994b
- Kawakami, Y., Eliyahu, S., Sakaguchi, K., Robbins, P. F., Rivoltini, L., Yannelli, J. R., Appella, E., and Rosenberg, S. A. Identification of the immunodominant peptides of the MART-1 human melanoma antigen recognized by the majority of HLA-A2-restricted tumor infiltrating lymphocytes. *J Exp Med* 180: 347-352, 1994c
- Khalil, I., D'Auriol, L., Gobet, M., Morin, L., Lepage, V., Deschamps, I., Park, M. S., Degos, L., Galibert, F., and Hors, J. A combination of HLA-DQ beta Asp57-negative and HLA DQ alpha Arg52 confers susceptibility to insulin-dependent diabetes mellitus. *J Clin Invest* 85: 1315-1319, 1990
- Khanna, R., Burrows, S. R., Kurilla, M. G., Jacob, C. A., Misko, I. S., Sculley, T. B., Kieff, E., and Moss, D. J. Localization of Epstein-Barr virus cytotoxic T cell epitopes using recombinant vaccinia: implications for vaccine development. *J Exp Med* 176: 169-176, 1992
- Kinouchi, R., Kobayashi, H., Sato, K., Kimura, S., and Katagiri, M. Peptide motifs of HLA-DR4/DR53 (DRB1*0405/DRB4*0101) molecules. *Immunogenetics* 40: 376-378, 1994
- Klavinskis, L. S., Whitton, J. L., Joly, E., and Oldstone, M. B. A. Vaccination and protection from a lethal viral infection: identification, incorporation, and use of a cytotoxic T lymphocyte glycoprotein epitope. *Virology* 178: 393-400, 1990
- Klein, J. Natural History of the Major Histocompatibility Complex. J. Wiley & Sons, New York, 1986
- Koenig, S., Fuerst, T. R., Wood, L. V., Woods, R. M., Suzich, J. A., Jones, G. M., De la Cruz, V. F., Davey, R. T., Jr., Venkatesan, S., Moss, B., Biddison, W. E., and Fauci, A. S. Mapping the fine specificity of a cytolytic T cell response to HIV-1 *nef* protein. *J Immunol* 145: 127-135, 1990
- Koziel, M. J., Dudley, D., Wong, J. T., Dienstag, J., Houghton, M., Ralston, R., and Walker, B. D. Intrahepatic cytotoxic T-lymphocytes specific for hepatitis-C virus in persons with chronic hepatitis. *J Immunol* 149: 3339-3344, 1992
- Kropshofer, H., Max, H., Müller, C. A., Hesse, F., Stevanović, S., Jung, G., and Kalbacher, H. Self-peptide released from class II HLA-DR1 exhibits a hydrophobic two-residue contact motif. *J Exp Med* 175: 1799-1803, 1992
- Kropshofer, H., Max, H., Halder, T., Kalbus, M., Müller, C. A., and Kalbacher, H. Self-peptides from four HLA-DR alleles share hydrophobic anchor residues near the NH2-terminal including proline as a stop signal for trimming. *J Immunol* 151: 4732-4742, 1993
- Kubo, R. T., Sette, A., Grey, H. M., Appella, E., Sakaguchi, K., Zhu, N. Z., Arnott, D., Sherman, N., Shabanowitz, J., Michel, H., Bodnar, W. M., Davis, T. A., and Hunt, D. F. Definition of specific peptide motifs for four major HLA-A alleles. *J Immunol* 152: 3913-3924, 1994
- Kulkarni, A. B., Morse, III, H. C., Bennink, J. R., Yewdell, J. W., and Murphy, B. R. Immunization of mice with vaccinia virus-M2 recombinant induces epitope-specific and cross-reactive K^d-restricted CD8⁺ cytotoxic-T cells. *J Virol* 67: 4086-4092, 1993
- Kumar, S., Miller, L. H., Quakyi, I. A., Keister, D. B., Houghten, R. A., Maloy, W. L., Moss, B., Berzofsky, J. A., and Good, M. F. Cytotoxic T cells specific for the circumsporozoite protein of *Plasmodium falciparum*. *Nature* 334: 258-260, 1988
- Kutubuddin, M., Simons, J., and Chow, M. Poliovirus-specific major histocompatibility complex class-I-restricted cytolytic T-cell epitopes in mice localize to neutralizing antigenic regions. *J Virol* 66: 5967-5974, 1992
- Kuwano, K., Braciale, T. J., and Ennis, F. A. Localization of a cross-reactive CTL epitope to the transmembrane region on the hemagglutinin of influenza H1 and H2 viruses. *FASEB J* 2: 2221, 1988
- Larson, J. K., Wunner, W. H., Olivos Jr., L., and Ertl, H. C. Identification of an immunodominant epitope within the phosphoprotein of rabies virus that is recognized by both class I- and class II-restricted T cells. *J Virol* 65: 5673-5679, 1991
- Lee, S. P., Thomas, W. A., Murray, R. J., Khanim, F., Faur, S., Young, L. S., Rowe, M., Kurilla, M., and Rickinson, A. B. HLA A2.1-restricted cytotoxic T-cells recognizing a range of Epstein-Barr virus isolates through a defined epitope in latent membrane protein LMP2. *J Virol* 67: 7428-7435, 1993
- Lethé, B., Van den Eynde, B., Van Pel, A., Corradin, G., and Boon, T. Mouse tumor rejection antigens P815A and antigen P815B: 2 epitopes carried by a single peptide. *Eur J Immunol* 22: 2283-2288, 1992
- Littau, R. A., Oldstone, M. B. A., Takeda, A., Debouck, C., Wong, J. T., Tuazon, C. U., Moss, B., Kievits, F., and Ennis, F. A. An HLA-C restricted CD8⁺ cytotoxic T lymphocyte clone recognizes a highly conserved epitope on human immunodeficiency virus type 1 gag. *J Virol* 65: 4051-4056, 1991
- Lurquin, C., Van Pel, A., Mariamé, B., De Plaen, E., Szikora, J.-P., Janssens, C., Reddehase, M. J., Lejeune, J., and Boon, T. Structure of the gene of tum-transplantation antigen P91A: the mutated exon encodes a peptide recognized with L^d by cytolytic T cells. *Cell* 58: 293-303, 1989
- Madden, D. R., Garboczi, D. N., and Wiley, D. C. The antigenic identity of peptide-MHC complexes - a comparison of the conformations of five viral peptides presented by HLA-A2. *Cell* 75: 693-708, 1993
- Maier, R., Falk, K., Rötzschke, O., Maier, B., Gnau, V., Stevanović, S., Jung, G., Rammensee, H.-G., and Meyerhans, A. Peptide motifs of HLA-A3, -A24, and -B7 molecules as determined by pool sequencing. *Immunogenetics* 40: 306-308, 1994
- Malcherek, G., Falk, K., Rötzschke, O., Rammensee, H.-G., Stevanović, S., Gnau, V., Jung, G., and Melms, A. Natural peptide ligand motifs of two HLA molecules associated with myasthenia gravis. *Int Immunol* 5: 1229-1237, 1993
- Mandelboim, O., Berke, G., Fridkin, M., Feldman, M., Eisenstein, M., and Eisenbach, L. CTL induction by a tumor-associated antigen octapeptide derived from a murine lung-carcinoma. *Nature* 369: 67-71, 1994
- Marrack, P., Ignatowicz, L., Kappler, J. W., Boymer, J., and Freed, J. H. Comparison of peptides bound to spleen and thymus class-II. *J Exp Med* 178: 2173-2183, 1993
- Martin, R., Howell, M. D., Jaraquemada, D., Flerlage, M., Richert, J., Brostoff, S., Long, E. O., McFarlin, D. E., and McFarland, H. F. A myelin basic protein peptide is recognized by cytotoxic T cells in the context of four HLA-DR types associated with multiple sclerosis. *J Exp Med* 173: 19-24, 1991
- Maryanski, J. L., Pala, P., Corradin, G., Jordan, B. R., and Cerottini, J.-C. H-2-restricted cytolytic T cells specific for HLA can recognize a synthetic HLA peptide. *Nature* 324: 578-579, 1986
- Matsushita, S., Takahashi, K., Motoki, M., Komoriya, K., Ikagawa, S., and Nishimura, Y. Allele specificity of structural requirement for peptides bound to HLA-DRB1*0405 and -DRB1*0406 complexes: implication for the HLA-associated susceptibility to methimazole-induced insulin autoimmune syndrome. *J Exp Med* 180: 873-883, 1994
- Missale, G., Redeker, A., Person, J., Fowler, P., Guilhot, S., Schlicht, H. J., Ferrari, C., and Chisari, F. V. HLA-A31- and HLA-Aw68-restricted cytotoxic T cell responses to a single hepatitis B virus nucleocapsid epitope during acute viral hepatitis. *J Exp Med* 177: 751-762, 1993
- Momburg, F., Neefjes, J. J., and Hammerling, G. J. Peptide selection by MHC-encoded Tap transporters. *Curr Opin Immunol* 6: 32-37, 1994
- Nayersina, R., Fowler, P., Guilhot, S., Missale, G., Cerny, A., Schlicht, H. J., Vitiello, A., Chesnut, R., Person, J. L., Redeker, A. G., and Chisari, F. V. HLA-A2 restricted cytotoxic T lymphocyte responses to multiple hepatitis B surface antigen epitopes during hepatitis B virus infection. *J Immunol* 150: 4659-4671, 1993
- Neefjes, J. J. and Momburg, F. Cell biology of antigen presentation. *Curr Opin Immunol* 5: 27-34, 1993
- Nelson, C. A., Roof, R. W., McCourt, D. W., and Unanue, E. R. Identification of the naturally processed form of hen egg white lysozyme bound to the murine major histocompatibility complex class II molecule I-A^k. *Proc Natl Acad Sci USA* 89: 7380-7383, 1992
- Newcomb, J. R. and Cresswell, P. Characterization of endogenous peptides bound to purified HLA-DR molecules and their absence

- from invariant chain-associated alpha-beta-dimers. *J Immunol* 150: 499–507, 1993
- Norda, M., Falk, K., Rötzschke, O., Stevanović, S., Jung, G., and Rammensee, H.-G. Comparison of the H-2K^b and H-2K^d restricted peptide motifs. *J Immunother* 14: 144–149, 1993
- O'Sullivan, D., Arrhenius, T., Sidney, J., Del Guercio, M.-F., Albertson, M., Wall, M., Oseroff, C., Southwood, S., Colon, S. M., Gaeta, F. C. A., and Sette, A. On the interaction of promiscuous antigenic peptides with different DR alleles. Identification of common structural motifs. *J Immunol* 147: 2663–2669, 1991
- Oldstone, M. B. A., Whitton, J. L., Lewicki, H., and Tishon, A. Fine dissection of a nine amino acid glycoprotein epitope, a major determinant recognized by lymphocytic choriomeningitis virus-specific class I-restricted H-2D^b cytotoxic T lymphocytes. *J Exp Med* 168: 559–570, 1988
- Oldstone, M. B. A., Tishon, A., Eddleston, M., De La Torre, J. C., McKee, T., and Whitton, J. L. Vaccination to prevent persistent viral infection. *J Virol* 67: 4372–4378, 1993
- Ortmann, B., Androlewicz, M. J., and Cresswell, P. MHC class I beta2-microglobulin complexes associate with Tap transporters before peptide binding. *Nature* 368: 864–867, 1994
- Pamer, E. G., Harty, J. T., and Bevan, M. J. Precise prediction of a dominant class I MHC-restricted epitope of *Listeria monocytogenes*. *Nature* 353: 852–855, 1991
- Pamer, E. G. Direct sequence identification and kinetic analysis of an MHC class I-restricted *Listeria monocytogenes* CTL epitope. *J Immunol* 152: 686–694, 1994
- Parker, K. C., Bednarek, M. A., and Coligan, J. E. Scheme for ranking potential HLA-A2 binding peptides based on independent binding of individual peptide side-chains. *J Immunol* 152: 163–175, 1994
- Pfeifer, J. D., Wick, M. J., Roberts, R. L., Findlay, K., Normark, S. J., and Harding, C. V. Phagocytic processing of bacterial antigens for class I MHC presentation to T cells. *Nature* 361: 359–362, 1993
- Phillips, R. E., Rowland-Jones, S., Huet, S., Hill, A., Sutton, J., Murray, R., Brooks, J., and McMichael, A. Human immunodeficiency virus genetic variation that can escape cytotoxic T cell recognition. *Nature* 354: 453–459, 1991
- Pinet, V., Malnati, M. S., and Long, E. O. Two processing pathways for the MHC class II-restricted presentation of exogenous influenza virus antigen. *J Immunol* 152: 4852–4860, 1994
- Rammensee, H.-G., Falk, K., and Rötzschke, O. Peptides naturally presented by MHC class I molecules. *Annu Rev Immunol* 11: 213–244, 1993
- Rawle, F. C., O'Connell, K. A., Geib, R. W., Roberts, B., and Gooding, L. R. Fine mapping of an H-2K^b restricted cytotoxic T lymphocyte epitope in SV 40 T antigen by using in-frame deletion mutants and a synthetic peptide. *J Immunol* 141: 2734–2739, 1988
- Reay, P. A., Kantor, R. M., and Davis, M. M. Use of global amino acid replacements to define the requirements for MHC binding and T cell recognition of moth cytochrome C (93–103). *J Immunol* 152: 3946–3957, 1994
- Reddehase, M. J., Rothbard, J. B., and Koszinowski, U. H. A pentapeptide as minimal antigenic determinant for MHC class I-restricted T lymphocytes. *Nature* 337: 651–653, 1989
- Reich, E. P., Von Grafenstein, H., Barlow, A., Swenson, K. E., Williams, K., and Janeway, C. A. Self peptides isolated from MHC glycoproteins of non-obese diabetic mice. *J Immunol* 152: 2279–2288, 1994
- Riberdy, J. M., Newcomb, J. R., Surman, M. J., Barbosa, J. A., and Cresswell, P. HLA-DR molecules from an antigen-processing mutant-cell line are associated with invariant chain peptides. *Nature* 360: 474–477, 1992
- Robbins, P. A., Lettice, L. A., Rota, P., Santos-Aguado, J., Rothbard, J., McMichael, A. J., and Strominger, J. L. Comparison between two peptide epitopes presented to cytotoxic T lymphocytes by HLA-A2. Evidence for discrete locations within HLA-A2. *J Immunol* 143: 4098–4103, 1989
- Robbins, P. F., Elgamil, M., Kawakami, Y., and Rosenberg, S. A. Recognition of tyrosinase by tumor-infiltrating lymphocytes from a patient responding to immunotherapy. *Cancer Res* 54: 3124–3126, 1994
- Rock, K. L., Rothstein, L., Gamble, S., and Fleischacker, C. Characterization of antigen-presenting cells that present exogenous antigens in association with class I MHC molecules. *J Immunol* 150: 438–446, 1993
- Rock, K. L., Gramm, C., Rothstein, L., Clark, K., Stein, R., Dick, L., Hwang, D., and Goldberg, A. L. Inhibitors of the proteasome block the degradation of most cell proteins and the generation of peptides presented on MHC class I molecules. *Cell* 78: 761–771, 1994
- Romero, P., Maryanski, J. L., Corradin, G., Nussenzweig, R. S., Nussenzweig, V., and Zavala, F. Cloned cytotoxic T cells recognize an epitope in the circumsporozoite protein and protect against malaria. *Nature* 341: 323–326, 1989
- Romero, P., Corradin, G., Luescher, J. F., and Maryanski, J. L. H-2K^d-restricted antigenic peptides share a simple binding motif. *J Exp Med* 174: 603–612, 1991
- Rötzschke, O., Falk, K., Deres, K., Schild, H., Norda, M., Metzger, J., Jung, G., and Rammensee, H.-G. Isolation and analysis of naturally processed viral peptides as recognized by cytotoxic T cells. *Nature* 348: 252–254, 1990
- Rötzschke, O., Falk, K., Stevanović, S., Jung, G., Walden, P., and Rammensee, H.-G. Exact prediction of a natural T cell epitope. *Eur J Immunol* 21: 2891–2894, 1991
- Rötzschke, O., Falk, K., Stevanović, S., Jung, G., and Rammensee, H.-G. Peptide motifs of closely related HLA class I molecules encompass substantial differences. *Eur J Immunol* 22: 2453–2456, 1992
- Rötzschke, O., Falk, K., Stevanović, S., Grahovac, B., Soloski, M. J., Jung, G., and Rammensee, H.-G. Qa-2 molecules are peptide receptors of higher stringency than ordinary class I molecules. *Nature* 361: 642–644, 1993
- Rötzschke, O., Falk, K., Stevanović, S., Gnau, V., Jung, G., and Rammensee, H.-G. Dominant aromatic/aliphatic C-terminal anchor in HLA-B*2702 and B*2705 peptide motifs. *Immunogenetics* 39: 74–77, 1994
- Rötzschke, O. and Falk, K. Origin, structure and motifs of naturally processed MHC class II ligands. *Curr Opin Immunol* 6: 45–51, 1994
- Rudensky, A. Y., Preston-Hurlburt, P., Hong, S.-C., Barlow, A., and Janeway, C. A. Sequence analysis of peptides bound to MHC class II molecules. *Nature* 353: 622–627, 1991
- Rudensky, A. Y., Preston-Hurlburt, P., Al-Ramadi, B. K., Rothbard, J., and Janeway, C. A. Truncation variants of peptides isolated from MHC class II molecules suggest sequence motifs. *Nature* 359: 429–431, 1992
- Ruppert, J., Sidney, J., Celis, E., Kubo, R. T., Grey, H. M., and Sette, A. Prominent role of secondary anchor residues in peptide binding to HLA-A2.1 molecules. *Cell* 74: 929–937, 1993
- Schulz, M., Aichele, P., Schneider, R., Hansen, T. H., Zinkernagel, R. M., and Hengartner, H. Major histocompatibility complex binding and T-cell recognition of a viral nonapeptide containing a minimal tetrapeptide. *Eur J Immunol* 21: 1181–1185, 1991
- Schumacher, T. N., De Bruijn, M. L., Vernie, L. N., Kast, W. M., Melief, C. J. M., Neefjes, J. J., and Ploegh, H. L. Peptide selection by MHC class I molecules. *Nature* 350: 703–706, 1991
- Sette, A., Buus, S., Appella, E., Smith, J. A., Chesnut, R., Miles, C., Colon, S. M., and Grey, H. M. Prediction of major histocompatibility complex binding regions of protein antigens by sequence pattern analysis. *Proc Natl Acad Sci USA* 86: 3296–3300, 1989
- Sette, A., Ceman, S., Kubo, R. T., Sakaguchi, K., Appella, E., Hunt, D. F., Davis, T. A., Michel, H., Shabanowitz, J., Rudersdorf, R., Grey, H. M., and DeMars, R. Invariant chain peptides in most HLA-DR molecules of an antigen-processing mutant. *Science* 258: 1801–1804, 1992
- Sette, A., Sidney, J., Oseroff, C., Del Guercio, M. F., Southwood, S., Arrhenius, T., Powell, M. F., Colon, S. M., Gaeta, F. C. A., and Grey, H. M. HLA DR4w4-binding motifs illustrate the biochemical basis of degeneracy and specificity in peptide-DR interactions. *J Immunol* 151: 3163–3170, 1993
- Sette, A., Sidney, J., Del Guercio, M. F., Southwood, S., Ruppert, J., Dahlberg, C., Grey, H. M., and Kubo, R. T. Peptide binding to the most frequent HLA-A class I alleles measured by quantitative molecular binding assays. *Mol Immunol* 31: 813–822, 1994

- Shawar, S. M., Vyas, J. M., Rodgers, J. R., Cook, R. G., and Rich, R. R. Specialized functions of major histocompatibility class I molecules. II. Hm1 binds N-formylated peptides of mitochondrial and procaryotic origin. *J Exp Med* 174: 941-944, 1991
- Shepherd, J. C., Schumacher, T. N. M., Ashton-Rickardt, P. G., Imaeda, S., Ploegh, H. L., Janeway, C. A., and Tonegawa, S. TAP1-dependent peptide translocation in vitro is ATP-dependent and peptide selective. *Cell* 74: 577-584, 1993
- Shirai, M., Okada, H., Nishioka, M., Akatsuka, T., Wychowski, C., Houghton, R., Pendleton, C. D., Feinstein, S. M., and Berzofsky, J. A. An epitope in hepatitis C virus core region recognized by cytotoxic T cells in mice and humans. *J Virol* 68: 3334-3342, 1994
- Sibille, C., Chomez, P., Wildmann, C., Van Pel, A., De Plaen, E., Maryanski, J. L., De Bergeyck, V., and Boon, T. Structure of the gene of tumour transplantation antigen P198: A point mutation generates a new antigenic peptide. *J Exp Med* 172: 35-45, 1990
- Sijts, A. J. A. M., Ossendorp, F., Mengede, E. A. M., Van den Elsen, P. J., and Melief, C. J. M. Immunodominant mink cell focus inducing murine leukemia virus (MuLV)-encoded CTL epitope, identified by its MHC class I binding motif, explains MuLV-type specificity of MCF-directed cytotoxic T lymphocytes. *J Immunol* 152: 106-116, 1994
- Silver, M. L., Guo, H. C., Strominger, J. L., and Wiley, D. C. Atomic structure of a human MHC molecule presenting an influenza-virus peptide. *Nature* 360: 367-369, 1992
- Sinigaglia, F. and Hammer, J. Defining rules for the peptide-MHC class II interaction. *Curr Opin Immunol* 6: 52-56, 1994
- Spouge, J. L., Guy, H. R., Cornette, J. L., Margalit, H., Cease, K., Berzofsky, J. A., and DeLisi, C. Strong conformational propensities enhance T cell antigenicity. *J Immunol* 138: 204-212, 1987
- Srivastava, P. K., Udono, H., Blachere, N. E., and Li, Z. H. Heat-shock proteins transfer peptides during antigen-processing and CTL priming. *Immunogenetics* 39: 93-98, 1994
- Starnbach, M. N. and Bevan, M. J. Cells infected with Yersinia present an epitope to class I MHC-restricted CTL. *J Immunol* 153: 1603-1612, 1994
- Stiern, L. J., Brown, J. H., Jardetzky, T. S., Gorga, J. C., Urban, R. G., Strominger, J. L., and Wiley, D. C. Crystal structure of the human class II MHC protein HLA-DR1 complexed with an influenza virus peptide. *Nature* 368: 215-221, 1994
- Stiern, L. J. and Wiley, D. C. Antigenic peptide binding by class I and class II histocompatibility proteins. *Structure* 2: 245-251, 1994
- Stevanović, S. and Rammensee, H.-G. The structure of T cell epitopes. In M. H. V. Van Regenmortel (ed). *Structure of Antigens*, in press
- Suh, W. K., Cohendoyle, M. F., Früh, K., Wang, K., Peterson, P. A., and Williams, D. B. Interaction of MHC class I molecules with the transporter associated with antigen processing. *Science* 264: 1322-1326, 1994
- Sutton, J., Rowland-Jones, S., Rosenberg, W., Nixon, D., Gotch, F., Gao, X.-M., Murray, N., Spoonas, A., Driscoll, P., Smith, M., Willis, A., and McMichael, A. A sequence pattern for peptides presented to cytotoxic T-lymphocytes by HLA-B8 revealed by analysis of epitopes and eluted peptides. *Eur J Immunol* 23: 447-453, 1993
- Sweetser, M. T., Morrison, L. A., Braciale, V. L., and Braciale, T. J. Recognition of pre-processed endogenous antigen by class I but not class II MHC-restricted T cells. *Nature* 342: 180-182, 1989
- Szikora, J. P., Van Pel, A., and Boon, T. Tumour mutation P35b generates the MHC-binding site of a new antigenic peptide. *Immunogenetics* 37: 135-138, 1993
- Takahashi, H., Cohen, J., Hosmalin, A., Cease, K. B., Houghton, R., Cornette, J. L., DeLisi, C., Moss, B., Germain, R. N., and Berzofsky, J. A. An immunodominant epitope of the human immunodeficiency virus envelope glycoprotein gp160 recognized by class I major histocompatibility complex molecule-restricted murine cytotoxic T lymphocytes. *Proc Natl Acad Sci USA* 85: 3105, 1988
- Takahashi, K., Dai, L. C., Fuerst, T., Biddison, W. E., Earl, P., Moss, B., and Ennis, F. A. Specific lysis of human immunodeficiency virus type 1-infected cells by a HLA-A3.1-restricted CD8 cytotoxic T lymphocyte clone that recognizes a conserved peptide sequence within the gp41 subunit of the envelope protein. *Proc Natl Acad Sci USA* 88: 10277-10281, 1991
- Tarpey, I., Stacey, S., Hickling, J., Birley, H. D. L., Renton, A., McIndoe, A., and Davies, D. H. Human cytotoxic T lymphocytes stimulated by endogenously processed human papillomavirus type 11 E7 recognize a peptide containing a HLA-A2 (A*0201) motif. *Immunology* 81: 222-227, 1994
- Tevethia, S. S., Lewis, M., Tanaka, Y., Milici, J., Knowles, B., Maloy, W. L., and Anderson, R. Dissection of H-2D^b-restricted cytotoxic T-lymphocyte epitopes on Simian virus 40 T antigen by the use of synthetic peptides and H-2D^b mutants. *J Virol* 64: 1192-1200, 1990
- Todd, J. A., Bell, J. I., and McDevitt, H. O. HLA-DQ beta gene contributes to susceptibility and resistance to insulin-dependent diabetes mellitus. *Nature* 329: 599-604, 1987
- Townsend, A., Ohlén, C., Bastin, J., Ljunggren, H.-G., Foster, L., and Kärre, K. Association of class I major histocompatibility heavy and light chains induced by viral peptides. *Nature* 340: 443-448, 1989
- Townsend, A., Ohlen, C., Rogers, M., Edwards, J., Mukherjee, S., and Bastin, J. Source of unique tumour antigens. *Nature* 371: 662, 1994
- Townsend, A. R., Rothbard, J., Gotch, F. M., Bahadur, G., Wraith, D., and McMichael, A. J. The epitopes of influenza nucleoprotein recognized by cytotoxic T lymphocytes can be defined with short synthetic peptides. *Cell* 44: 959-968, 1986
- Traversari, C., Van der Bruggen, P., Luescher, I. F., Lurquin, C., Chomez, P., Van Pel, A., De Plaen, E., Amar-Costesec, A., and Boon, T. A nonapeptide encoded by human gene *MAGE-1* is recognized on HLA-A1 by cytolytic T lymphocytes directed against tumor antigen MZ2-E. *J Exp Med* 176: 1453-1457, 1992
- Udaka, K., Tsomides, T. J., and Eisen, H. N. A naturally occurring peptide recognized by alloreactive CD8⁺ cytotoxic T lymphocytes in association with a class I protein. *Cell* 69: 989-998, 1992
- Udaka, K., Tsomides, T. J., Walden, P., Fukusen, N., and Eisen, H. N. A ubiquitous protein is the source of naturally occurring peptides that are recognized by a CD8⁺ T-cell clone. *Proc Natl Acad Sci USA* 90: 11272-11276, 1993
- Urban, R. G., Chic, R. M., Lane, W. S., Strominger, J. L., Rehm, A., Kenter, M. J. H., Uytdehaag, F. G. C. M., Ploegh, H., Uchanska-Ziegler, B., and Ziegler, A. A subset of HLA-B27 molecules contains peptides much longer than nonamers. *Proc Natl Acad Sci USA* 91: 1534-1538, 1994
- Utz, U., Koenig, S., Coligan, J. E., and Biddison, W. E. Presentation of three different viral peptides, HTLV-1 Tax, HCMV gB, and influenza virus M1, is determined by common structural features of the HLA-A2.1 molecule. *J Immunol* 149: 214-221, 1992
- Van Binnendijk, R. S., Versteeg van Oosten, J. P., Poelen, M. C., Brugghe, H. F., Hoogerhout, P., Osterhaus, A. D., and Uytdehaag, F. G. Human HLA class I- and HLA class II-restricted cloned cytotoxic T lymphocytes identify a cluster of epitopes on the measles virus fusion protein. *J Virol* 67: 2276-2284, 1993
- Van Bleek, G. M. and Nathanson, S. G. Isolation of an immunodominant viral peptide from the class I H-2K^b molecule. *Nature* 348: 213-216, 1990
- Van der Bruggen, P., Traversari, C., Chomez, P., Lurquin, C., De Plaen, E., Van den Eynde, B., Knuth, A., and Boon, T. A gene encoding an antigen recognized by cytolytic T-lymphocytes on a human melanoma. *Science* 254: 1643-1647, 1991
- Venet, A. and Walker, B. D. Cytotoxic T-cell epitopes in HIV SIV Infection. *Aids* 7: S117-S126, 1993
- Vogt, A. B., Kropshofer, H., Kalbacher, H., Kalbus, M., Rammensee, H.-G., Coligan, J. E., and Martin, R. Ligand motifs of HLA-DRB5*0101 and DRB1*1501 molecules delineated from self-peptides. *J Immunol* 153: 1665-1673, 1994
- Von Boehmer, H. Thymic selection - a matter of life and death. *Immunol Today* 13: 454-458, 1992
- Walker, B. D., Flexner, C., Birch-Limberger, K., Fisher, L., Paradis, T. J., Aldovini, A., Young, R., Moss, B., and Schooley, R. T. Long-term culture and fine specificity of human cytotoxic T-lymphocyte clones reactive with human immunodeficiency virus type. *Proc Natl Acad Sci USA* 86: 9514-9518, 1989

- Wallny, H.-J. Untersuchungen zur Rolle der MHC-Klasse-I-Moleküle bei der Prozessierung von Nebenhistokompatibilitätsantigenen. Dissertation; Universität Tübingen, 1992
- Wallny, H.-J., Deres, K., Faath, S., Jung, G., Van Pel, A., Boon, T., and Rammensee, H.-G. Identification and quantification of a naturally presented peptide as recognized by cytotoxic T lymphocytes specific for an immunogenic tumor variant. *Int Immunol* 4: 1085-1090, 1992
- Wei, M. L. and Cresswell, P. HLA-A2 molecules in an antigen processing mutant cell contain signal sequence derived peptides. *Nature* 356: 443-446, 1992
- Weiss, W. R., Mellouk, S., Houghten, R. A., Sedegah, M., Kumar, S., Good, M. F., Berzofsky, J. A., Miller, L. H., and Hoffmann, S. L. Cytotoxic T cells recognize a peptide from the circumsporozoite protein on malaria-infected hepatocytes. *J Exp Med* 171: 763-773, 1990
- White, H. D., Roeder, D. A., and Green, W. R. An immunodominant K^b-restricted peptide from the P15E transmembrane protein of endogenous ecotropic murine leukemia-virus (Mulv) Akr623 that restores susceptibility of a tumor line to anti-AKR Gross.MULV cytotoxic T-lymphocytes. *J Virol* 68: 897-904, 1994
- Whitton, J. L., Tishon, A., Lewicki, H., Gebhard, J., Cook, T., Salvato, M., Joly, E., and Oldstone, M. B. A. Molecular analyses of a five-amino-acid cytotoxic T-lymphocyte (CTL) epitope: an immunodominant region which induces nonreciprocal CTL cross-reactivity. *J Virol* 63: 4303-4310, 1989
- Wölfel, T., Van Pel, A., Brichard, V., Schneider, J., Seliger, B., Zum Büschenfelde, K. H. M., and Boon, T. 2 tyrosinase nonapeptides recognized on HLA-A2 melanomas by autologous cytolytic T-Lymphocytes. *Eur J Immunol* 24: 759-764, 1994
- Wucherpfennig, K. W., Sette, A., Southwood, S., Oseroff, C., Matsui, M., Strominger, J. L., and Hafler, D. A. Structural requirements for binding of an immunodominant myelin basic protein peptide to DR2 isotypes and for its recognition by human T cell clones. *J Exp Med* 179: 279-290, 1994
- Yanagi, Y., Tishon, A., Lewicki, H., Cubitt, B. A., and Oldstone, M. B. A. Diversity of T cell receptors in virus specific cytotoxic T lymphocytes recognizing 3 distinct viral epitopes restricted by a single major histocompatibility complex molecule. *J Virol* 66: 2527-2531, 1992
- Zhang, Q. J., Gavioli, R., Klein, G., and Masucci, M. G. An HLA-A11-specific motif in nonamer peptides derived from viral and cellular proteins. *Proc Natl Acad Sci USA* 90: 2217-2221, 1993
- Zhang, W., Young, A. C. M., Imarai, M., Nathanson, S. G., and Sacchettini, J. C. Crystal structure of the major histocompatibility complex class I H-2K^b molecule containing a single viral peptide: implications for peptide binding and T-cell receptor recognition. *Proc Natl Acad Sci USA* 89: 8403-8407, 1992



Merriam-Webster
OnLine



Cheap!
The Best Kept Secret

Merriam-Webster **FOR KIDS**

Encyclopædia **BRITANNICA**

Merriam-Webster **ONLINE**

Merriam-Webster **COLLEGIATE**

Merriam-Webster **UN**

HOME

PREMIUM SERVICES ▼

M-WCollegiate.com
M-WUnabridged.com
Britannica.com
Multi-User Licenses

DOWNLOADS ◀

WORD OF THE DAY ◀

WORD GAMES ◀

WORD FOR THE WISE ◀

ONLINE STORE ◀

HELP ◀

Merriam-Webster Inc.
Company information

Merriam-Webster Online Dictionary

One entry found for **composition**.

Thesaurus

Merriam-Webster

Ⓒ **Dictionary**

○ **Thesaurus**



composition

Main Entry: **com·po·si·tion** ㄏ

Pronunciation: "käm-p&- 'zi-sh&n

Function: *noun*

Etymology: Middle English *composicioun*, from Middle French *composition*, from Latin *composition-*, *compositio*, from *componere*

1 a : the act or process of composing; *specifically* : arrangement into specific proportion or relation and especially into artistic form **b (1)** : the arrangement of type for printing <hand *composition*> **(2)** : the production of type or typographic characters (as in photocomposition) arranged for printing

2 a : the manner in which something is composed **b** : general makeup <the changing ethnic *composition* of the city -- Leonard Buder> **c** : the qualitative and quantitative makeup of a chemical compound

3 : mutual settlement or agreement

4 : a product of mixing or combining various elements or ingredients

5 : an intellectual creation: as **a** : a piece of writing; *especially* : a school exercise in the form of a brief essay **b** : a written piece of music especially of considerable size and complexity

6 : the quality or state of being compound

7 : the operation of forming a composite function; *also* : **COMPOSITE FUNCTION**

- **com·po·si·tion·al** ㄏ /-'zish-n&l, -'zi-sh&-n&l/
adjective

- **com·po·si·tion·al·ly** *adverb*

For **More Information** on "**composition**" go to [Britannica.com](http://www.britannica.com)

Get the **Top 10 Search Results** for "**composition**"

Pronunciation Symbols

Palm & Pock

Browse and download
Merriam-Webster
e-books and game
Palm and Pocket P
and Mobile Phones
[Merriam-Webster
Online Store](http://www.merriam-webster.com/online-store)

**Handheld
Collegiate**

Now you can take
Eleventh Edition w
anywhere as Frankl
new Speaking Elec
Handheld!
[Franklin.com/](http://www.franklin.com/)

**Merriam-Webster
Collegiate
14-day Free**

From:AOYAMA & PARTNERS

国際様式

INTERNATIONAL FORM

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT

issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page.

特許手続上の微生物の寄託の国際的承認
に関するブダペスト条約

下記国際寄託当局によって規則7.1に従い
発行される。

原寄託についての受託証

氏名 (名称)

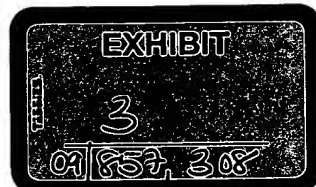
伊東 恭悟

殿

寄託者

あて名

佐賀県三養基郡基山町けやき台2-25-9



1. 微生物の表示

(寄託者が付した識別のための表示)

E. coli JM109 (3D9)

(受託番号)

FERM BP- 6929

2. 科学的性質及び分類学上の位置

1株の微生物には、次の事項を記載した文書が添付されていた。

- 科学的性質
- 分類学上の位置

3. 受領及び受託

本国際寄託当局は、平成10年11月25日(原寄託日)に受領した1株の微生物を受託する。

4. 移管請求の受領

本国際寄託当局は、平成10年11月25日(原寄託日)に1株の微生物を受領した。
そして、平成11年11月4日に原寄託よりブダペスト条約に基づく寄託への移管請求を受領した。
(平成10年11月25日に寄託された微工研函寄第P-17062号より移管)

5. 国際寄託当局

通商産業省工業技術院生命工学工業技術研究所

名称: National Institute of Bioscience and Human-Technology
Agency of Industrial Science and Technology

所長 大箸 信

Dr. Shinobu Oshikiri Director-General

あて名: 日本国茨城県つくば市東1丁目1番3号(郵便番号305-8566)

1-3, Higashi 1 chome Tsukuba-shi Ibaraki-ken
305-8566, JAPAN

平成11年(1999)11月4日

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT

issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page.

特許手続上の微生物の寄託の国際的承認
に関するブタベスト条約

下記国際寄託当局によって規則7.1に従い
発行される。

原寄託についての受託証

氏名 (名称)

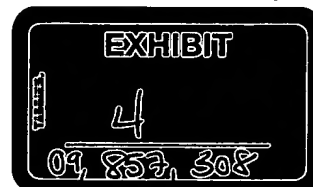
伊東 恭悟

寄託者

あて名

佐賀県三養基郡基山町けやき台2-25-9

股



1. 微生物の表示

(寄託者が付した識別のための表示)
KG-CTL

(受託番号)
FERM BP- 6725

2. 科学的性質及び分類学上の位置

1 棚の微生物には、次の事項を記載した文書が添付されていた。

- 科学的性質
- 分類学上の位置

3. 受領及び受託

本国際寄託当局は、平成10年 6月19日(原寄託日)に受領した1棚の微生物を受託する。

4. 移管請求の受領

本国際寄託当局は、平成10年 6月19日(原寄託日)に1棚の微生物を受領した。
そして、平成11年 5月20日に原寄託よりブタベスト条約に基づく寄託への移管請求を受領した。
(平成10年 6月19日に寄託された微生物研菌寄第P-16854号より移管)

5. 国際寄託当局

通商産業省工業技術院生命工学工業技術研究所

名称: National Institute of Advanced Industrial Science and Technology
Agency of Industrial Science and Technology

所長 大築 信

Dr. Shinobu Ohtsuki Director-General

あて名: 日本国茨城県つくば市東上町1番3号 (郵便番号305-8566)
1-3, Higashi 1 chome Tsukuba-shi Ibaraki-ken
305-8566, JAPAN

平成11年(1999) 5月20日

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT

issued pursuant to Rule 7.1 by the INTERNATIONAL DEPOSITARY AUTHORITY identified at the bottom of this page.

特許手続上の微生物の寄託の国際的承認
に関するブダペスト条約

下記国際寄託当局によって規則7.1に従い
発行される。

原寄託についての受託証

氏名 (名称)

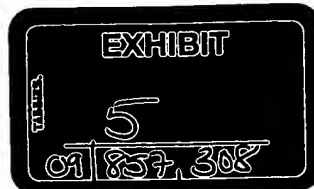
伊東 恭悟

寄託者

あて名 〒

佐賀県三養基郡基山町けやき台2-25-9

殷



1. 微生物の表示

(寄託者が付した識別のための表示)
食通菌細胞株KE-4

(受託番号)
FERM BP- 5955

2. 科学的性質及び分類学上の位置

1 棚の微生物には、次の事項を記載した文書が添付されていた。

- 科学的性質
- 分類学上の位置

3. 受領及び受託

本国際寄託当局は、平成 9 年 5 月 23 日 (原寄託日) に受領した1棚の微生物を受託する。

4. 移管請求の受領

本国際寄託当局は、年 月 日 (原寄託日) に1棚の微生物を受領した。
そして、年 月 日に原寄託よりブダペスト条約に基づく寄託への移管請求を受領した。

5. 国際寄託当局

通商産業省工業技術院生命工学工業技術研究所

名称: National Institute of Advanced Industrial Science and Technology
Agency of Industrial Science and Technology

所長 太石 道夫

Michio . DIRECTOR GENERAL.

あて名: 日本国茨城県つくば市東1丁目1番3号 (郵便番号305)
1-3, Higashi 1 chome Tsukuba-shi Ibaraki-ken
305, JAPAN

平成 9 年 (1997) 5月23日

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☒ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.